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INITIAL SUBMISSION: A CLOSED-PATCH REPEATED INSULT DERMAL SENSITIZATION STUDY IN GUINEA PIGS WITH TOLUENE DIISOCYANATE AND OTHERS WITH COVER LETTER DATED 051592		
Chemical Category		
TOLUENE DIISOCYANATE		

8(e)

CAP

(COMPLIANCE AUDIT PROGRAM)

4/1/2

**TSCA CONFIDENTIAL
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American Cyanamid Company
One Cyanamid Plaza
Wayne, NJ 07470

H. Michael D. Utidjian, M.D.
Corporate Medical Director

May 15, 1992

8EHQ-0592-4112 Init

CERTIFIED MAIL
RETURN RECEIPT REQUESTED



88920002754

Document Processing Center (TS-790)
Office of Toxic Substances
Environmental Protection Agency
401 M Street, S.W.
Washington, D.C. 20460

Att'n: Section 8(e) Coordinator (CAP Agreement)

RE: Study or Report Submitted Pursuant to the TSCA
Section 8(e) Compliance Audit Program

Identification Number: 8ECAP-0041

Dear Sir/Madam:

American Cyanamid Company is submitting the attached study to the Environmental Protection Agency (EPA) pursuant to the Toxic Substances Control Act (TSCA) Section 8(e) Compliance Audit Program (CAP Agreement) executed by American Cyanamid and EPA. This study does not involve effects observed in humans. These documents do not contain confidential business information.

The enclosed study provides information on the following chemical substances:

Toluene diisocyanate (TDI)
(80% 2,4-[CAS 584-84-9])
(20% 2,6-[CAS 91-08-7])
4,4'-Methylenediphenyl diisocyanate (MDI) [CAS 101-68-0]
p-tetramethylxylene diisocyanate (p-TMXDI) [CAS 2778-41-8]
Isophorone diisocyanate (IPDI) [CAS 4091-71-9]
m-tetramethylxylene diisocyanate (m-TMXDI) [CAS 2778-42-9]
Hydrogenated 4,4'-methylenediphenyl diisocyanate (HMDI)
[CAS 5124-30-1]
3(-2-propenyl)-1-(2-propyl-2-isocyanato) benzene (m-TMI)
[CAS 2094-99-7]

The title of the enclosed report is "A Closed-Patch Repeated Insult Dermal Sensitization Study in Guinea Pigs With TDI, MDI, p-TMXDI, IPDI, m-TMXDI, HMDI and m-TMI (Modified Buehler Method)," December 20, 1984.

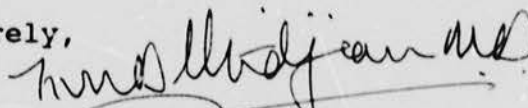
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Under the conditions of the study, all of these materials except MD1 produced sensitization in guinea pigs.

In total, American Cyanamid is submitting three (3) copies of the enclosed report and this cover letter: an original and two (2) copies.

Further questions regarding this submission may be directed to Ms. Patricia A. Vernon, Associate Toxicologist at the address above or 201-831-2534.

Sincerely,

A handwritten signature in dark ink, appearing to read "H. Michael D. Utidjian". The signature is fluid and cursive, with a horizontal line drawn across the bottom of the name.

H. Michael D. Utidjian, M.D.
Corporate Medical Director

CONTAINS NO CBI



Bio/dynamics Inc.

Division of Biology and Safety Evaluation

PROJECT NO.: 4971-84

A CLOSED-PATCH REPEATED INSULT
DERMAL SENSITIZATION STUDY IN GUINEA PIGS WITH
TDI, MDI, p-TMXDI, IPDI, m-TMXDI, HMDI and m-TMI
(Modified Buehler Method)

Submitted to: American Cyanamid Company
One Cyanamid Plaza
Wayne, New Jersey 07470

Attn: Dr. Richard Davis

Date: December 20, 1984

TABLE OF CONTENTS

I.	INTRODUCTION.....	1
II.	DATES OF STUDY.....	1
III.	STUDY PERSONNEL.....	1
IV.	EXPERIMENTAL DESIGN.....	2
V.	MATERIALS	
	A. Test and Control Materials.....	3
	B. Test Animals.....	4
VI.	METHODS	
	A. Route of Administration.....	6
	B. Justification for Route of Administration.....	6
	C. Duration of Study.....	6
	D. Schedule.....	6
	E. Range-Finding Study.....	6
	F. Doses.....	7
	G. Pretest Procedures, Preparation of Animals.....	7
	H. Preparation of Test Materials.....	7
	I. Administration of Test Materials.....	7
VII.	EXPERIMENTAL EVALUATION	
	A. Viability Check.....	9
	B. General Observations.....	9
	C. Evaluation of Dermal Response.....	9
VIII.	POST-MORTEM/STUDY TERMINATION	
	A. Blood Collection.....	9
	B. Animal Termination.....	9
IX.	RESULTS AND DISCUSSION	
	A. Mortality and General Observations.....	10
	B. Dermal Responses.....	10
X.	CONCLUSION.....	14

TABLE OF CONTENTS (CONT.)

TABLES

IA	Summary of Responses to Induction Exposures.....	15
IB	Individual Dermal Scores at Induction.....	22
IIA	Incidence of Dermal Response at Challenge.....	43
IIB	Summary of Responses to Challenge.....	44
IIC	Individual Dermal Scores at Challenge.....	51
IIIA	Summary of Responses to Cross-challenge.....	79
IIIB	Individual Dermal Scores at Cross-challenge.....	82

APPENDICES

A	Range-finding Data.....	A-1
B	Dermal Evaluation Scoring Scale.....	B-1
C	Quality Assurance Statement.....	C-1

I. INTRODUCTION

This study was conducted for the American Cyanamid Company in order to define the dose-response curve of TDI, MDI, p-TMXDI, IPDI, m-TMXDI, HMDI and m-TMI for induction of dermal sensitization in guinea pigs and for subsequent challenge and to determine the potential for inducing cross-sensitization to structurally related materials. This study was performed at Bio/dynamics, Inc., Mettlers Road, East Millstone, New Jersey 08873, and used procedures based on the methods described by E.V. Buehler in "Delayed Contact Hypersensitivity in the Guinea Pig", Arch. Dermatol 91: 171-175 (1965) and H.L. Ritz and E.V. Buehler in "Planning, Conduct and Interpretation of Guinea Pig Sensitization Patch Tests", in Current Concepts in Cutaneous Toxicity (Victor A. Drill and Paul Lazar, eds.), pp. 25-40; Academic Press, 1980.

This report has been reviewed by the Quality Assurance Unit of Bio/dynamics, Inc. to assure its conformance with the protocol and the raw data. All raw data and the original study protocol and final report will be retained on file in the Bio/dynamics Archives.

II. DATES OF STUDY

Animal Receipt:	April 2, 1984
Range-Finding:	April 10, 12 and 13, 1984
Induction: (First through Third Inductions)	April 24 through May 8, 1984
Challenge:	May 22, 1984
Cross-challenge:	May 29, 1984
Study Termination:	May 31, 1984

III. STUDY PERSONNEL

Study Director:	Carol S. Auletta, B.A., D.A.B.T.
Supervisor:	Donna L. Blaszcak, B.S., AALAS, R.L.A.T.
Technician-in-Charge:	Janet Erickson, A.A.S., AALAS, L.A.T.
Report preparation:	Donna L. Blaszcak, B.S., AALAS, R.L.A.T.

IV. EXPERIMENTAL DESIGN

Group	Material	Dose	Number of Animals ^a	Induction Concentration (milliMolar)	Challenge Concentrations (milliMolar)	Cross-Challenge ^c		Serum Samples	Animals Shipped ^d
						Materials	Concentration (milliMolar)		
I	A TDI	Low	15	30	90,30,9,0.9,0.09	none	none	yes	no
	B TDI	Middle	15	90	90,30,9,0.9,0.09	none	none	yes	yes
	C TDI	High	15	300	90,30,9,0.9,0.09	p-TMXDI, m-TMXDI, m-TMI, HMDI	60, 30, 150, 30	yes	no
	D TDI	Control-C ^b	6	none	90,30,9,0.9,0.09	none	none	no	no
	E e	Control-XC ^b	e	none	none	p-TMXDI, m-TMXDI, m-TMI, HMDI	60, 30, 150, 30	no	no
II	A HMDI	Low	15	10	30,10,3,0.3,0.03	none	none	yes	no
	B HMDI	Middle	15	30	30,10,3,0.3,0.03	none	none	yes	yes
	C HMDI	High	15	100	30,10,3,0.3,0.03	p-TMXDI, m-TMXDI, m-TMI, IPDI	60, 30, 150, 30	yes	no
	D HMDI	Control-C ^b	6	none	30,10,3,0.3,0.03	none	none	no	no
	E e	Control-XC ^b	e	none	none	p-TMXDI, m-TMXDI, m-TMI, TDI	60, 30, 150, 90	no	no
III	A p-TMXDI	Low	15	20	60,20,6,0.6,0.06	none	none	yes	no
	B p-TMXDI	Middle	15	60	60,20,6,0.6,0.06	none	none	yes	yes
	C p-TMXDI	High	15	200	60,20,6,0.6,0.06	IPDI, m-TMXDI, HMDI, m-TMI	90, 30, 60, 150	yes	no
	D p-TMXDI	Control-C ^b	6	none	60,20,6,0.6,0.06	none	none	no	no
	E e	Control-XC ^b	e	none	none	IPDI, m-TMXDI, HMDI, m-TMI	90, 30, 60, 150	no	no
IV	A IPDI	Low	15	30	90,30,9,0.9,0.09	none	none	yes	no
	B IPDI	Middle	15	90	90,30,9,0.9,0.09	none	none	yes	yes
	C IPDI	High	15	300	90,30,9,0.9,0.09	p-TMXDI, m-TMXDI, HMDI, m-TMI	60, 30, 60, 150	yes	no
	D IPDI	Control-C ^b	6	none	90,30,9,0.9,0.09	none	none	no	no
	E e	Control-XC ^b	e	none	none	p-TMXDI, m-TMXDI, HMDI, m-TMI	60, 30, 60, 150	no	no
V	A m-TMXDI	Low	15	10	30,10,3,0.3,0.03	none	none	yes	no
	B m-TMXDI	Middle	15	30	30,10,3,0.3,0.03	none	none	yes	yes
	C m-TMXDI	High	15	100	30,10,3,0.3,0.03	p-TMXDI, IPDI, HMDI, m-TMI	60, 90, 60, 150	yes	no
	D m-TMXDI	Control-C ^b	6	none	30,10,3,0.3,0.03	none	none	no	no
	E e	Control-XC ^b	e	none	none	p-TMXDI, IPDI, HMDI, m-TMI	60, 90, 60, 150	no	no
VI	A HMDI	Low	15	20	60,20,6,0.6,0.06	none	none	yes	no
	B HMDI	Middle	15	60	60,20,6,0.6,0.06	none	none	yes	yes
	C HMDI	High	15	200	60,20,6,0.6,0.06	p-TMXDI, IPDI, m-TMXDI, m-TMI	60, 90, 30, 150	yes	no
	D HMDI	Control-C ^b	6	none	60,20,6,0.6,0.06	none	none	no	no
	E e	Control-XC ^b	e	none	none	p-TMXDI, IPDI, m-TMXDI, m-TMI	60, 90, 30, 150	no	no
VII	A m-TMI	Low	15	50	150,50,15,1.5,0.15	none	none	yes	no
	B m-TMI	Middle	15	150	150,50,15,1.5,0.15	none	none	yes	yes
	C m-TMI	High	15	500	150,50,15,1.5,0.15	p-TMXDI, IPDI, m-TMXDI, HMDI	60, 90, 30, 60	yes	no
	D m-TMI	Control-C ^b	6	none	150,50,15,1.5,0.15	none	none	no	no
	E e	Control-XC ^b	e	none	none	p-TMXDI, IPDI, m-TMXDI, HMDI	60, 90, 30, 60	no	no

^aThe 15 animals in the test material-treated groups were divided approximately equally by sex, i.e., 7 males and 8 females or 8 males and 7 females. The six animals in the control group were 3 males and 3 females.

^bControl animals did not receive induction exposures. Challenge control animals (C) were treated at challenge only; cross-challenge control animals (XC) were treated at cross-challenge only.

^cSingle concentrations of 4 different structurally related materials were administered at cross-challenge to each animal in the high-dose (Sub-group C) and to cross-challenge control (Sub-group E) animals.

^dSelected animals were shipped after study termination, at the sponsor's request, to Dr. John H. Wallace at the University of Louisville, Louisville, Kentucky.

^eSingle concentrations of four materials were administered at cross-challenge to one group of six animals and single concentrations of the other three materials were administered to a second group of six animals for a total of 12 animals.

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-3-
4971-84MATERIALSA. Test and Control Materials:1. Test Materials:

Abbreviation	Test Material	Molecular Weight	Description	Date of Receipt (1984)	Received From American Cyanamid Co. (Location)
TDI	Toluene diisocyanate (80% 2,4-; 20% 2,6-)	174	Clear colorless liquid	3/23	Bound Brook, N.J.
MDI	4,4'-Methylenediphenyl diisocyanate	250	Clear colorless liquid	3/23	Bound Brook, N.J.
p-TMXDI	para-tetramethylxylene diisocyanate	244	Off-white solid	3/22	Stamford, CT.
IPDI	Isophorone diisocyanate	222	Clear colorless liquid	3/28	Bound Brook, N.J.
m-TMXDI	Meta tetramethylxylene diisocyanate	244	Clear colorless liquid	3/22	Stamford, CT.
HMDI	Hydrogenated 4,4'-methylenediphenyl diisocyanate	262	Clear colorless liquid	3/23	Bound Brook, N.J.
m-TMI	3(-2-propenyl)-1-(2-propyl-2-isocyanato) benzene	201	Clear, light yellow liquid	3/22	Stamford, CT.

Storage: All materials were stored at room temperature under a nitrogen blanket.

2. Vehicles:

a. Acetone HPLC (Anhydrous)

Lot Number: 237099
Description: Clear colorless liquid
Supplier: J.T. Baker Chemical Company
Phillipsburg, New Jersey
Storage: Room temperature, under nitrogen blanket

b. Olive Oil Progresso Pure Imported Olive Oil

Lot Number: 1083-A
Description: Slightly viscous amber liquid
Supplier: Progresso Company
Storage: Room temperature

V. MATERIALS (cont.)

B. Test Animals: Guinea Pigs

Stock: Hartley Albino

Reason for Selection: Standard laboratory animal for dermal sensitization studies. The Hartley Albino breed is used because of its availability and because of the existing historical data base for comparative evaluation.

Number of Animals:

1. Range-finding:
60 (30 males, 30 females)
2. Sensitization Study:
315 (158 males, 157 females)
3. Irritation Controls:
Challenge: 42 (21 males, 21 females)
Cross-challenge: 12 (6 males, 6 females)

Supplier: Hazleton-Dutchland Laboratory Animals
Denver, PA

Age: 3-4 weeks at receipt
5-6 weeks old at study initiation

Weight Range at Initiation
of Treatment
(Sensitization Study
Animals):

Males:	307-480 grams
Females:	299-462 grams

Equilibration Period: Range-finding: 8 - 11 days
Sensitization Study: 22 days

Observations: All animals were checked for viability twice daily. Prior to assignment to study all animals received a physical examination to ascertain suitability for study.

Husbandry: Currently acceptable practices of good animal husbandry were followed, e.g., Guide for the Care and Use of Laboratory Animals; DHEW Publication No. (NIH) 78-23 Revised 1978.

V. MATERIALS (cont.)

Housing: Individually in suspended stainless steel cages.

Room Assignments: Animals were housed in two rooms as follows:

<u>Room No.</u>	<u>Groups</u>
1	I, II, III, IV A-C
2	V, VI, VII, A-E I, II, III, IV D-E

Food: Agway Prolab Guinea Pig Diet, ad libitum.

Water: Automatic watering system, ad libitum
(Elizabethtown Water Company).

- Environmental Conditions:
1. Temperature: 65-75°F is considered an acceptable temperature range for guinea pigs; room temperature was monitored and recorded twice daily and maintained within this range to the maximum extent possible.
 2. Humidity: 30-70% is considered an acceptable humidity range for guinea pigs; humidity was monitored and recorded daily and maintained within this range to the maximum extent possible.
 3. Light Cycle: 12 hours light, 12 hours dark (controlled by an automatic timer).

Animal Identification: Each animal was identified with a unique number designated on the cage card.

Selection: Animals were randomly placed in cages upon receipt and were placed on study as available. Those of questionable health or with outlying body weights or unacceptable skin were not placed on study.

VI. METHODSA. Route of Administration:

Dermal, to the clipped skin of the back and sides.

B. Justification for Route of Administration:

The study is intended to provide information on the health hazards likely to arise from exposure to the test material by the dermal route; skin contact is a possible worker and consumer exposure route. The Buehler method is an acceptable method for evaluating the potential of test materials to produce dermal sensitization.

C. Duration of Study:

Range-finding Study: 3-6 days
Sensitization Study: 37 days

D. Schedule:

This test consists of three segments, 1) attempted induction of sensitization, 2) challenge of animals to evaluate presence and/or extent of sensitization and 3) cross-challenge with structurally-related materials to evaluate potential for producing cross-sensitization. The following summary describes the sequence of steps. Detailed information is presented below.

Weeks 1 to 3 - Induction of sensitization, by closed-patch technique, once weekly for 3 weeks.

Week 5 - Challenge

Week 6 - Cross-challenge

E. Range-Finding Study:

Prior to initiation of the study, an irritation range-finding study was performed in order to select a vehicle and doses for the induction and challenge applications.

Six animals per test material were treated topically with concentrations of 1.0, 0.3, 0.1, 0.03, 0.01 and 0.003 Molar of the test material in 100% Olive Oil or in a 1:1 mixture of olive oil and anhydrous acetone. The test material mixtures were applied directly to the skin and covered with an adhesive-backed gauze patch (Elastoplast® Coverlet Spot or Oval) in a volume of 30 microliters. The patches were then occluded with impermeable plastic and secured by an elastic adhesive bandage (Elastoplast®) which was wound around the torso of the animal. The patches were left in place for six hours, after which they were removed and the skin was wiped free of any excess material. Observations for irritation were made 24 and 48 hours after application and again at Day 4, 5 or 6. At each observation, all treated sites were scored using the scoring system in Appendix B.

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VI. METHODS (cont.)F. Doses:

Based on results of the range-finding study (presented in Appendix A concentrations were selected as outlined in the Experimental Design (Section IV).

G. Pretest, Procedures, Preparation of Animals:1. Blood Sample:

A blood sample was collected from the toenail bed of each test animal (by clipping) 1 to 8 days prior to study initiation. Blood was allowed to clot, i.e., no anticoagulants were used. Serum was obtained, frozen and shipped to Dr. John H. Wallace at the University of Louisville, Louisville, Kentucky (Blood samples were not obtained from irritation control animals - sub-groups D and E). Approximately 0.5 ml of blood (0.1 ml of serum) was required from each animal.

2. Dermal Preparation:

The hair on the application site (back and sides) was clipped short with an electric clipper on the day prior to each induction application and prior to challenge and cross-challenge.

H. Preparation of Test Materials:

Liquids were diluted and solids were dissolved in a 1:1 mixture of olive oil and anhydrous acetone. For induction, 1M concentrations were prepared on the day prior to dosing and diluted on the day of administration. For challenge, 0.1 or 0.2M concentrations were prepared and diluted on the day prior to dosing. For re-challenge, 0.1 or 0.2M concentrations were prepared on the day prior to dosing and diluted on the day of administration. Care was taken to avoid any contact of the test material with moisture, i.e., glassware was thoroughly dried and test materials and the anhydrous acetone were kept under a nitrogen blanket after opening.

I. Administration of Test Materials:1. Induction:

Materials were administered in a volume of 50 microliters beneath an adhesive-backed gauze patch (Elastoplast® Coverlet Oval) placed directly on the test site. The test site was on the anterior portion of the right side of the animal. The patch was covered by overlapping, impermeable plastic and firmly secured by an elastic adhesive bandage wound around the torso of the animal. The patch was left in place for 6 hours after which it was removed and the skin wiped free of any excess material. This was repeated at the same site once weekly for 3 weeks, for a total of 3 applications.

VI. METHODS (cont.)I. Administration of Test Materials (cont.):2. Challenge:

Fourteen days after the last induction exposure, the challenge treatment was administered. Five different concentrations were administered, at sites on the opposite side of the midline from the site used for induction (i.e., on the left side) 25 microliters of each concentration was applied beneath a small adhesive-backed gauze patch (Elastoplast® Coverlet Spot). The five patches were then covered by impermeable plastic and firmly secured by an elastic adhesive bandage wrapped around the torso. After six hours of exposure, the patches were removed and the skin wiped free of any excess material. In order to differentiate possible dermal reactions produced by irritation from those produced by sensitization, 6 animals (previously untreated but from same lot as the test animals) were subjected to the same challenge procedure as the animals which had received the induction exposures.

3. Cross-Challenge:

In order to evaluate the potential for cross reactivity with structurally related materials, single concentrations of 4 different materials were applied to the high dose (Sub-group C) test animals (See Experimental Design) upon recovery from challenge (seven days after challenge). A previously untreated site (the posterior portion of the right side) was used. Cross-challenge control animals (previously untreated but from the same lot as the test animals) were also treated with these materials and concentrations. Twelve irritation control animals were needed (6 test sites per animal).

VII. EXPERIMENTAL EVALUATION

A. Viability Check:

Twice Daily

B. General Observations:

Prior to treatment and weekly during study.

C. Evaluation of Dermal Response:

1. Intervals:

Induction:

Dermal evaluations of the induction site were made prior to dosing and approximately 24 hours after each induction application.

Challenge and Cross-Challenge:

Dermal evaluations of the challenge site were made prior to dosing and approximately 24 and 48 hours after the challenge applications.

2. Methods:

Reactions were scored according to the system in Appendix B.

VIII. POST-MORTEM/STUDY TERMINATION

A. Blood Collection:

A blood sample was collected from each test animal after challenge (3 or 4 days after the challenge dose). (Blood samples were not obtained from irritation control animals). The procedure was the same as that used prior to test. Serum was obtained, frozen and shipped to the University of Louisville, Louisville, Kentucky. Approximately 0.5 ml of blood (0.1 ml of serum) was required from each animal.

B. Animal Termination:

All animals in the mid-dose groups (Sub-group B) were shipped (alive) to Dr. John H. Wallace at the University of Louisville, Louisville, Kentucky after the termination of the study (June 6, 1984). All other surviving animals were killed and discarded without necropsy examinations.

IX. RESULTS AND DISCUSSIONA. Mortality and General Observations

All animals survived through termination of the study. The majority of animals were free of abnormalities throughout the study. One animal (No. 2758, male, Group IIIA) sustained a mechanical injury to its foot and two animals (No. 2874, male, Group VIIB and No. 2862, male, Group VIIC) were noted to have swollen and/or reddened feet, possibly indicative of infections subsequent to the pretest blood collection. One female (No. 3042, Group IIIC) was noted to have red mucous discharge from the ano-genital area on Day 7 and another female (No. 3127, Group VIIA) exhibited ocular irritation on Day 7.

B. Dermal Responses1. Induction (Summary - Table IA, Individual Scores - (Table IB)

Concentrations selected for induction were non-irritating for all low-and mid-dose (A and B) sub-groups, as demonstrated by a lack of significant dermal response to these concentrations after the initial induction exposure. Induction concentrations for most high-dose (C) sub-groups were minimally irritating upon initial administration, although no irritation was seen for the high-dose concentration of MDI (Group IIC). Some residual irritation from previous application(s) was apparent as a predose observation for the second and third induction exposures. This occurred primarily in the high-dose subgroups and was most pronounced in the groups receiving p-TMXDI and m-TMI.

Responses generally increased in incidence and severity after subsequent induction exposures; dermal scores after the third exposure were generally higher than those seen after the first exposure. Incidence and severity of response were concentration-dependent. This type of response to repeated exposures may represent a cumulative irritant effect and/or may be indicative of sensitization.

IX. RESULTS AND DISCUSSION (cont.)B. Dermal Responses (cont.)1. Induction (cont.)

Animals treated with MDI showed the lowest degree of change in scores over the induction period and those treated with TDI showed a slightly higher degree of change. Changes were more marked for animals treated with the other five materials (p-TMXDI, IPDI, m-TMXDI, HMDI and m-TMI). These results are consistent with those seen after the challenge application.

2. Challenge (Summaries - Tables IIA and IIB, Individual Scores - Table IIC)

Dermal scores at challenge of 1 or greater (in the absence of dermal response in irritation control animals) are considered clearly indicative of sensitization. Scores of + (barely perceptible, usually non-confluent, erythema) are considered equivocal, although a high percentage of scores of + in treated animals with no dermal response in irritation control animals is considered suggestive of sensitization.

Numbers of animals exhibiting dermal scores of + or higher and of animals exhibiting scores of 1 or higher after treatment with five different challenge concentrations are presented in Table IIA.

Challenge applications were made to previously untreated skin. All concentrations administered at challenge were non-irritating, as confirmed by a lack of significant dermal response in irritation control animals and by a similar lack of response by the test animals to the initial induction applications. (The two highest challenge concentrations were the same as the low- and mid-dose induction concentrations).

IX. RESULTS AND DISCUSSION (cont.)

B. Dermal Responses (cont.)

2. Challenge (cont.)

Dermal sensitization was apparent for all test materials, with the possible exception of MDI. Incidence and severity of response were dependent upon both the induction and the challenge concentration for all but the MDI-treated groups.

Animals treated with low, mid or high induction concentrations of MDI exhibited minimal responses (2/15, 4/15 or 5/15 animals per group with scores of +) to high challenge concentrations of this material. Questionable responses (scores of +) were also seen in 1/15 and 3/15 low induction-concentration animals to mid and mid-high challenge concentrations, respectively. Only one definitive response (dermal score of 1) was seen for this material; this was noted in an animal which received a low induction concentration in response to challenge with a mid-high concentration. These data suggest that MDI possesses some potential to produce dermal sensitization in the guinea pig. However, higher induction and/or challenge concentrations may be necessary to elicit a more definitive response.

Animals treated with TDI exhibited slightly clearer responses, although the incidence of animals responding was low. Definitive responses (scores of 1 or greater) were seen in 2/15 mid-dose and 3/15 high-dose animals, respectively, to a high challenge concentration. Minimal responses (scores of + or greater) to the high challenge concentration were seen in 2/15, 8/15 and 7/15 low-, mid- and high-dose animals, respectively; minimal responses to the mid-high challenge concentration were also seen in 2/15 high-dose animals. These responses confirm the sensitization potential of TDI. However, higher induction and challenge concentrations might elicit more definitive responses.

Revised Page: 2. J. Amato Date: 2/20/85

IX. RESULTS AND DISCUSSION (cont.)B. Dermal Responses (cont.)2. Challenge (cont.)

Dose-related responses to mid-high and high challenge concentrations were apparent for animals treated with all three induction concentrations of the other five materials (p-TMXDI, IPDI, m-TMXDI, HMDI and m-TMI). Responses to lower challenge concentrations were generally sporadic and minimal.

3. Cross-Challenge (Summary - Table IIIA, Individual Scores - Table IIIB)

Some cross-sensitization potential was seen for p-TMXDI, m-TMI, IPDI, m-TMXDI and HMDI. Animals sensitized to another test material and challenged with one of these materials exhibited responses suggestive of or indicative of cross-sensitization. Incidence and severity of response was generally low. p-TMXDI elicited the strongest cross-sensitization response, with m-TMI eliciting slightly lower responses. Cross-sensitization to IPDI, m-TMXDI and HMDI was generally low and comparable for these three materials. No cross-sensitization to TDI or MDI was apparent for any of the test materials. No significant dermal response was seen in irritation control animals.

X. CONCLUSION

Under conditions of this study, p-TMXDI, IPDI, m-TMXDI, HMDI and m-TMI exhibited the potential to produce dermal sensitization in guinea pigs and to produce cross-sensitization to structurally related materials. Incidence and severity of response were dependent upon both induction and challenge concentrations. p-TMXDI and m-TMI elicited the strongest cross-sensitization responses. TDI exhibited some potential to produce dermal sensitization but no apparent potential to produce cross-sensitization. MDI elicited responses suggestive of sensitization but exhibited no apparent potential to produce cross-sensitization.

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TABLE IA
A CLOSED-PATCH REPEATED INSULT DERMAL SENSITIZATION STUDY IN
GUINEA PIGS

SUMMARY OF RESPONSES TO INDUCTION EXPOSURES^a

GROUP: I

MATERIAL: TDI

Induction Number	Interval	Group	Conc. (mM)	Dermal Scores							N	D
				0	+	1	2	3	Ed			
1	Pre-dose	I	A 30	15	-	-	-	-	-	-	-	-
			B 90	15	-	-	-	-	-	-	-	-
			C 300	15	-	-	-	-	-	-	-	-
	24 Hours	I	A 30	14	1	-	-	-	-	-	-	-
			B 90	14	1	-	-	-	-	-	-	-
			C 300	7	7	1	-	-	-	-	-	-
2	Pre-dose	I	A 30	15	-	-	-	-	-	-	-	-
			B 90	12	3	-	-	-	-	-	-	-
			C 300	4	10	1	-	-	-	-	-	3
	24 Hours	I	A 30	13	2	-	-	-	-	-	-	-
			B 90	-	3	9	3	-	1	-	-	-
			C 300	-	-	4	10	1	6	-	-	-
3	Pre-dose	I	A 30	11	4	-	-	-	-	-	-	1
			B 90	6	9	-	-	-	-	-	-	10
			C 300	-	8	7	-	-	-	-	-	12
	24 Hours	I	A 30	9	5	1	-	-	-	-	-	-
			B 90	1	5	8	1	-	1	-	-	1
			C 300	-	1	5	9	-	9	-	-	1

^aNumbers presented are numbers of animals with indicated score. See Appendix B for scoring system. N=15 per group.

TABLE IA (cont.)

A CLOSED-PATCH REPEATED INSULT DERMAL SENSITIZATION STUDY IN
GUINEA PIGS

SUMMARY OF RESPONSES TO INDUCTION EXPOSURES^a

GROUP: II

MATERIAL: MDI

Induction Number	Interval	Group	Conc. (mM)	Dermal Scores					Ed	N	D
				0	+	1	2	3			
1	Pre-dose	II	A 10	15	-	-	-	-	-	-	-
			B 30	15	-	-	-	-	-	-	-
			C 100	15	-	-	-	-	-	-	-
	24 Hours	II	A 10	14	1	-	-	-	-	-	-
			B 30	15	-	-	-	-	-	-	-
			C 100	15	-	-	-	-	-	-	-
2	Pre-dose	II	A 10	15	-	-	-	-	-	-	-
			B 30	15	-	-	-	-	-	-	-
			C 100	14	1	-	-	-	-	-	-
	24 Hours	II	A 10	14	1	-	-	-	-	-	-
			B 30	13	2	-	-	-	-	-	-
			C 100	5	9	1	-	-	-	-	-
3	Pre-dose	II	A 10	12	3	-	-	-	-	-	-
			B 30	11	4	-	-	-	-	-	1
			C 100	8	7	-	-	-	-	-	4
	24 Hours	II	A 10	12	1	2	-	-	-	-	-
			B 30	9	5	1	-	-	-	-	-
			C 100	5	8	2	-	-	-	-	-

^aNumbers presented are numbers of animals with indicated score. See Appendix B for scoring system. N=15 per group.

TABLE IA (cont.)

A CLOSED-PATCH REPEATED INSULT DERMAL SENSITIZATION STUDY IN
GUINEA PIGS

SUMMARY OF RESPONSES TO INDUCTION EXPOSURES^a

GROUP: III

MATERIAL: p-TMXDI

Induction Number	Interval	Group	Conc. (mM)	Dermal Scores							
				0	+	1	2	3	Ed	N	D
1	Pre-dose	III A	20	15	-	-	-	-	-	-	-
		B	60	15	-	-	-	-	-	-	-
		C	200	15	-	-	-	-	-	-	-
	24 Hours	III A	20	15	-	-	-	-	-	-	-
		B	60	11	4	-	-	-	-	-	-
		C	200	0	8	7	-	-	5	-	-
2	Pre-dose	III A	20	15	-	-	-	-	-	-	-
		B	60	14	1	-	-	-	-	-	-
		C	200	2	8	3	2	-	2	-	5
	24 Hours	III A	20	3	2	5	5	-	2	-	-
		B	60	-	1	4	9	1	6	-	-
		C	200	-	-	-	10	5	14	1	-
3	Pre-dose	III A	20	8	6	1	-	-	-	-	9
		B	60	2	12	1	-	-	-	-	14
		C	200	-	6	7	1	1	1	1	14 ^b
	24 Hours	III A	20	3	3	1	8	-	3	-	2
		B	60	-	-	7	8	-	3	-	1
		C	200	-	-	1	10	4	13	1	-

^aNumbers presented are numbers of animals with indicated score. See Appendix B for scoring system. N=15 per group.

^bOne animal also exhibited exfoliation.

TABLE IA (cont.)

A CLOSED-PATCH REPEATED INSULT DERMAL SENSITIZATION STUDY IN
GUINEA PIGS

SUMMARY OF RESPONSES TO INDUCTION EXPOSURES^a

GROUP: IV

MATERIAL: IPDI

Induction Number	Interval	Group	Conc. (mM)	Dermal Scores							N	D
				0	+	1	2	3	Ed			
1	Pre-dose	IV	A 30	15	-	-	-	-	-	-	-	-
			B 90	15	-	-	-	-	-	-	-	-
			C 300	15	-	-	-	-	-	-	-	-
	24 Hours	IV	A 30	15	-	-	-	-	-	-	-	-
			B 90	15	-	-	-	-	-	-	-	-
			C 300	2	12	1	-	-	2	-	-	-
2	Pre-dose	IV	A 30	15	-	-	-	-	-	-	-	-
			B 90	13	2	-	-	-	-	-	-	-
			C 300	11	3	1	-	-	-	-	-	5
	24 Hours	IV	A 30	4	7	4	-	-	-	-	-	-
			B 90	1	3	5	6	-	7	-	-	-
			C 300	-	-	-	13	2	15	-	-	-
3	Pre-dose	IV	A 30	8	7	-	-	-	-	-	-	3
			B 90	3	10	2	-	-	-	-	-	9
			C 300	-	9	6	-	-	-	-	-	13
	24 Hours	IV	A 30	3	8	3	-	1	1	1	-	-
			B 90	-	-	9	6	-	7	-	-	3
			C 300	-	-	1	11	3	12	1	-	-

^aNumbers presented are numbers of animals with indicated score. See
Appendix B for scoring system. N=15 per group.

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TABLE IA (cont.)

A CLOSED-PATCH REPEATED INSULT DERMAL SENSITIZATION STUDY IN
GUINEA PIGS

SUMMARY OF RESPONSES TO INDUCTION EXPOSURES^a

GROUP: V

MATERIAL: m-TMXDI

Induction Number	Interval	Group	Conc. (mM)	Dermal Scores							
				0	+	1	2	3	Ed	N	D
1	Pre-dose	V	A 10	15	-	-	-	-	-	-	-
			B 30	15	-	-	-	-	-	-	-
			C 100	15	-	-	-	-	-	-	-
	24 Hours	V	A 10	15	-	-	-	-	-	-	-
			B 30	15	-	-	-	-	-	-	-
			C 100	8	7	-	-	-	-	-	-
2	Pre-dose	V	A 10	15	-	-	-	-	-	-	-
			B 30	15	-	-	-	-	-	-	-
			C 100	13	2	-	-	-	-	-	-
	24 Hours	V	A 10	14	1	-	-	-	-	-	-
			B 30	4	5	4	2	-	-	-	-
			C 100	-	-	7	8	-	8	-	-
3	Pre-dose	V	A 10	14	1	-	-	-	-	-	-
			B 30	8	6	1	-	-	-	-	4
			C 100	-	8	7	-	-	-	-	6
	24 Hours	V	A 10	9	5	1	-	-	-	-	-
			B 30	1	4	6	4	-	3	-	-
			C 100	-	-	1	12	2	14	-	-

^aNumbers presented are numbers of animals with indicated score. See Appendix B for scoring system. N=15 per group.

TABLE IA (cont.)

A CLOSED-PATCH REPEATED INSULT DERMAL SENSITIZATION STUDY IN
GUINEA PIGS

SUMMARY OF RESPONSES TO INDUCTION EXPOSURES^a

GROUP: VI

MATERIAL: HMDI

Induction Number	Interval	Group	Conc. (mM)	Dermal Scores							N	D
				0	+	1	2	3	Ed			
1	Pre-dose	VI	A 20	15	-	-	-	-	-	-	-	-
			B 60	15	-	-	-	-	-	-	-	-
			C 200	15	-	-	-	-	-	-	-	-
	24 Hours	VI	A 20	15	-	-	-	-	-	-	-	-
			B 60	15	-	-	-	-	-	-	-	-
			C 200	9	4	2	-	-	-	-	-	-
2	Pre-dose	VI	A 20	15	-	-	-	-	-	-	-	-
			B 60	11	4	-	-	-	-	-	-	-
			C 200	8	7	-	-	-	-	-	-	5
	24 Hours	VI	A 20	9	5	1	-	-	-	-	-	-
			B 60	-	2	8	5	-	4	-	-	-
			C 200	-	-	-	10	5	14	-	-	-
3	Pre-dose	VI	A 20	10	5	-	-	-	-	-	-	1
			B 60	4	8	3	-	-	-	-	-	13
			C 200	-	8	7	-	-	-	-	-	12
	24 Hours	VI	A 20	7	3	5	-	-	-	-	-	-
			B 60	1	-	6	8	-	5	-	-	-
			C 200	-	-	-	11	4	14	1	-	-

^aNumbers presented are numbers of animals with indicated score. See Appendix B for scoring system. N=15 per group.

TABLE IA (cont.)

A CLOSED-PATCH REPEATED INSULT DERMAL SENSITIZATION STUDY IN
GUINEA PIGS

SUMMARY OF RESPONSES TO INDUCTION EXPOSURES^a

GROUP: VII

MATERIAL: m-TMI

Induction Number	Interval	Group	Conc. (mM)	Dermal Scores							N	D
				0	+	1	2	3	Ed			
1	Pre-dose	VII A	50	15	-	-	-	-	-	-	-	-
		B	150	15	-	-	-	-	-	-	-	-
		C	500	15	-	-	-	-	-	-	-	-
	24 Hours	VII A	50	15	-	-	-	-	-	-	-	-
		B	150	15	-	-	-	-	-	-	-	-
		C	500	3	11	1	-	-	2	-	-	-
2	Pre-dose	VII A	50	15	-	-	-	-	-	-	-	-
		B	150	15	-	-	-	-	-	-	-	-
		C	500	1	8	5	1	-	1	-	-	11
	24 Hours	VII A	50	15	-	-	-	-	-	-	-	-
		B	150	2	5	7	1	-	2	-	-	-
		C	500	-	-	-	13	2	15	-	-	-
3	Pre-dose	VII A	50	13	2	-	-	-	-	-	-	1
		B	150	9	6	-	-	-	-	-	-	5
		C	500	-	1	10	3	1	1	1 ^b	-	15
	24 Hours	VII A	50	9	3	2	1	-	-	-	-	-
		B	150	1	2	7	4	1	2	-	-	-
		C	500	-	-	-	2	13	15	7	-	-

^aNumbers presented are numbers of animals with indicated score. See Appendix B for scoring system. N=15 per group.

^bA second animal exhibited foci of necrosis.

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TABLE 1B

A CLOSED-PATCH REPEATED INSULT DERMAL SENSITIZATION STUDY IN
GUINEA PIGS

INDIVIDUAL DERMAL SCORES^a AT INDUCTION

GROUP: 1A

INDUCTION MATERIAL: YDI
CONCENTRATION: 30 mM

Animal No. and Sex	Induction 1		Induction 2		Induction 3	
	Pre-Dose	24 Hours	Pre-Dose	24 Hours	Pre-Dose	24 Hours
2750 M	0	0	0	0	+	0
2751 M	0	0	0	0	0	+
2753 M	0	0	0	0	0	0
2754 M	0	0	0	+	+	+
2755 M	0	0	0	0	0	0
2756 M	0	0	0	0	+	+
2757 M	0	0	0	0	0	0
2758 M	0	0	0	0	0	0
2998 F	0	+	0	0	0	0
2999 F	0	0	0	+	+,D	1
3164 F	0	0	0	0	0	+
3002 F	0	0	0	0	0	0
3003 F	0	0	0	0	0	0
3004 F	0	0	0	0	0	0
3006 F	0	0	0	0	0	+

^aScored using the scale presented in Appendix B.

M=Male

F=Female

D=Desquamation

TABLE IB (cont.)

A CLOSED-PATCH REPEATED INSULT DERMAL SENSITIZATION STUDY IN
GUINEA PIGS

INDIVIDUAL DERMAL SCORES^a AT INDUCTION

GROUP: IB INDUCTION MATERIAL: TDI
CONCENTRATION: 90 mM

Animal No. and Sex	Induction 1		Induction 2		Induction 3	
	Pre-Dose	24 Hours	Pre-Dose	24 Hours	Pre-Dose	24 Hours
2799 M	0	0	+	1	+,D	+
2800 M	0	0	0	2,Ed	+,D	1,D
2801 M	0	+	0	2	+,D	1
2802 M	0	0	0	2	0,D	2
2803 M	0	0	0	+	0	0
2804 M	0	0	0	1	0	1
2805 M	0	0	0	1	+	+
2806 M	0	0	0	+	+	1
3047 F	0	0	0	+	0,D	+
3048 F	0	0	0	1	+,D	+
3049 F	0	0	0	1	+,D	1,Ed
3050 F	0	0	+	1	0,D	+
3051 F	0	0	0	1	+	1
3052 F	0	0	+	1	0,D	1
3053 F	0	0	0	1	+,D	1

^aScored using the scale presented in Appendix B.

M=Male

F=Female

D=Desquamation

Ed=Edema

TABLE 1B (cont.)

A CLOSED-PATCH REPEATED INSULT DERMAL SENSITIZATION STUDY IN
GUINEA PIGS

INDIVIDUAL DERMAL SCORES^a AT INDUCTION

GROUP: IC INDUCTION MATERIAL: TDI
CONCENTRATION: 300 mM

Animal No. and Sex	Induction 1		Induction 2		Induction 3	
	Pre-Dose	24 Hours	Pre-Dose	24 Hours	Pre-Dose	24 Hours
2807 M	0	+	0	2	1	1,Ed
2808 M	0	0	0	1	+	1
2809 M	0	+	+	2,Ed	1,D	2,Ed
2810 M	0	0	0	2	+,D	2
2811 M	0	1	+,D	2	1,D	2
2812 M	0	0	+	1	+,D	2,Ed
2813 M	0	0	+	2	+,D	+
3054 F	0	+	+	2,Ed	1,D	1,Ed
3055 F	0	+	+	2,Ed	+	1,Ed
3056 F	0	0	+	1	1,D	2,Ed
3134 F	0	+	+,D	2,Ed	+,D	2
3058 F	0	+	+,D	2,Ed	+,D	2,Ed
3059 F	0	+	+	2	1,D	2,Ed,D
3060 F	0	0	1	3,Ed	1,D	2,Ed
3061 F	0	0	0	1	+,D	1

^aScored using the scale presented in Appendix B.

M=Male

F=Female

D=Desquamation

Ed=Edema

TABLE IB (cont.)

A CLOSED-PATCH REPEATED INSULT DERMAL SENSITIZATION STUDY IN
GUINEA PIGS

INDIVIDUAL DERMAL SCORES^a AT INDUCTION

GROUP: IIA INDUCTION MATERIAL: MDI
CONCENTRATION: 10 mM

Animal No. and Sex	Induction 1		Induction 2		Induction 3	
	Pre-Dose	24 Hours	Pre-Dose	24 Hours	Pre-Dose	24 Hours
2759 M	0	0	0	0	0	0
2760 M	0	0	0	0	0	0
2762 M	0	0	0	0	0	+
2763 M	0	0	0	+	+	1
2764 M	0	0	0	0	0	0
2765 M	0	0	0	0	0	0
2766 M	0	0	0	0	0	0
3007 F	0	+	0	0	+	1
3008 F	0	0	0	0	0	0
3009 F	0	0	0	0	0	0
3010 F	0	0	0	0	0	0
3011 F	0	0	0	0	0	0
3012 F	0	0	0	0	0	0
3013 F	0	0	0	0	0	0
3014 F	0	0	0	0	+	0

^aScored using the scale presented in Appendix B.

M=Male

F=Female

TABLE 1B (cont.)

A CLOSED-PATCH REPEATED INSULT DERMAL SENSITIZATION STUDY IN
GUINEA PIGS

INDIVIDUAL DERMAL SCORES^a AT INDUCTION

GROUP: IIB INDUCTION MATERIAL: MDI
CONCENTRATION: 30 mM

Animal No. and Sex	Induction 1		Induction 2		Induction 3	
	Pre-Dose	24 Hours	Pre-Dose	24 Hours	Pre-Dose	24 Hours
2767 M	0	0	0	0	+	+
2768 M	0	0	0	0	0	0
2769 M	0	0	0	0	0	0
2770 M	0	0	0	0	0	0
2771 M	0	0	0	0	0	0
2772 M	0	0	0	0	0	0
2773 M	0	0	0	+	0	+
2774 M	0	0	0	0	0	0
3015 F	0	0	0	+	+	+
3016 F	0	0	0	0	0	0
3017 F	0	0	0	0	+,D	1
3018 F ^{ph}	0	0	0	0	0	+
3019 F	0	0	0	0	0	0
3020 F	0	0	0	0	0	0
3021 F	0	0	0	0	+	+

^aScored using the scale presented in Appendix B.

M=Male
F=Female

TABLE 1B (cont.)

A CLOSED-PATCH REPEATED INSULT DERMAL SENSITIZATION STUDY IN
GUINEA PIGS

INDIVIDUAL DERMAL SCORES^a AT INDUCTION

GROUP: IIC INDUCTION MATERIAL: MDI
CONCENTRATION: 100 mM

Animal No. and Sex	Induction 1		Induction 2		Induction 3	
	Pre-Dose	24 Hours	Pre-Dose	24 Hours	Pre-Dose	24 Hours
2775 M	0	0	0	+	+	+
2776 M	0	0	0	+	0	0
2777 M	0	0	+	0	0	+
2778 M	0	0	0	0	0	0
2779 M	0	0	0	0	+	+
2780 M	0	0	0	+	0,D	+
2781 M	0	0	0	1	+,D	1
3022 F	0	0	0	0	0	0
3023 F	0	0	0	+	+,D	+
3135 F	0	0	0	+	+,D	+
3025 F	0	0	0	+	+	0
3026 F	0	0	0	+	0	1
3027 F	0	0	0	+	0	0
3028 F	0	0	0	+	0	+
3029 F	0	0	0	0	+	+

^aScored using the scale presented in Appendix B.

M=Male

F=Female

D=Desquamation

TABLE IB (cont.)

A CLOSED-PATCH REPEATED INSULT DERMAL SENSITIZATION STUDY IN
GUINEA PIGS

INDIVIDUAL DERMAL SCORES^a AT INDUCTION

GROUP: IIIA INDUCTION MATERIAL: p-TMXDI
CONCENTRATION: 20 mM

Animal No. and Sex	Induction 1		Induction 2		Induction 3	
	Pre-Dose	24 Hours	Pre-Dose	24 Hours	Pre-Dose	24 Hours
2743 M	0	0	0	1	+,D	2
2744 M	0	0	0	+	0	0
2745 M	0	0	0	1	0,D	+,D
2746 M	0	0	0	0	+,D	2
2747 M	0	0	0	0	0	0
2748 M	0	0	0	1	+,D	2,Ed
2749 M	0	0	0	2,Ed	0	+,D
2989 F	0	0	0	2	+,D	2
2990 F	0	0	0	2,Ed	1,D	2,Ed
2991 F	0	0	0	+	0	0
2992 F	0	0	0	2	0,D	2
2993 F	0	0	0	1	0	2
2994 F	0	0	0	1	+,D	2,Ed
2995 F	0	0	0	2	+,D	+
2997 F	0	0	0	0	0	1

^aScored using the scale presented in Appendix B.

M=Male

F=Female

D=Desquamation

Ed=Edema

TABLE IB (cont.)

A CLOSED-PATCH REPEATED INSULT DERMAL SENSITIZATION STUDY IN
GUINEA PIGS

INDIVIDUAL DERMAL SCORES^a AT INDUCTION

GROUP: IIIB

INDUCTION MATERIAL: p-TMXDI
CONCENTRATION: 60 mM

Animal No. and Sex	Induction 1		Induction 2		Induction 3	
	Pre-Dose	24 Hours	Pre-Dose	24 Hours	Pre-Dose	24 Hours
2782 M	0	0	0	1	+	1
2783 M	0	+	0	2	+,D	1
2784 M	0	0	0	2,Ed	+,D	2,Ed
2785 M	0	0	0	2	+,D	2
2788 M	0	0	0	1	+,D	1
2789 M	0	0	0	2,Ed	+,D	1,D
2790 M	0	0	0	2,Ed	+,D	2,Ed
2791 M	0	0	0	+	+,D	1
3030 F	0	0	+	3	1,D	2
3031 F	0	0	0	1	+,D	2
3033 F	0	+	0	2,Ed	+,D	2,Ed
3034 F	0	0	0	2	0,D	1
3035 F	0	+	0	2,Ed	+,D	1
3036 F	0	0	0	1	0,D	2
3037 F	0	+	0	2,Ed	+,D	2

^aScored using the scale presented in Appendix B.

M=Male

F=Female

D=Desquamation

Ed=Edema

TABLE IB (cont.)

A CLOSED-PATCH REPEATED INSULT DERMAL SENSITIZATION STUDY IN
GUINEA PIGS

INDIVIDUAL DERMAL SCORES^a AT INDUCTION

GROUP: IIIC INDUCTION MATERIAL: p-TMXDI
CONCENTRATION: 200 mM

Animal No. and Sex	Induction 1		Induction 2		Induction 3	
	Pre-Dose	24 Hours	Pre-Dose	24 Hours	Pre-Dose	24 Hours
2792 M	0	1	1	3,Ed	1,D	2,Ed
2793 M	0	+	1	2,Ed	1,D	2,Ed
2794 M	0	1,Ed	2,Ed	3,Ed,N	3,N,Ex, Ed,Db	2,Ed
2795 M	0	1,Ed	+	3,Ed	1,D	3,Ed
2796 M	0	1,Ed	2,Ed	3,Ed	2,D	3,Ed,N
2797 M	0	+	1	2,Ed	1	2,Ed
2798 M	0	+	+,D	2,Ed	+,D	2,Ed
3038 F	0	+	0	2,Ed	+,D	2,Ed
3039 F	0	1,Ed	+,D	2,Ed	1,D	2,Ed
3040 F	0	+	+,D	3,Ed	+,D	3,Ed
3041 F	0	1	+,D	2,Ed	+,D	2,Ed
3042 F	0	+	0,D	2,Ed	+,D	2
3044 F	0	+	+	2,Ed	1,D	3,Ed
3045 F	0	+	+	2,Ed	1,D	1
3046 F	0	1,Ed	+	2	+,D	2,Ed

^aScored using the scale presented in Appendix B.

^bBecause of tissue damage (necrosis) the patch for the third induction was placed at a new site (over undamaged skin).

M=Male

F=Female

D=Desquamation

Ed=Edema

N=Necrosis

Ex=Exfoliation

TABLE IB (cont.)

A CLOSED-PATCH REPEATED INSULT DERMAL SENSITIZATION STUDY IN
GUINEA PIGS

INDIVIDUAL DERMAL SCORES^a AT INDUCTION

GROUP: IVA INDUCTION MATERIAL: IPDI
CONCENTRATION: 30 mM

Animal No. and Sex	Induction 1		Induction 2		Induction 3	
	Pre-Dose	24 Hours	Pre-Dose	24 Hours	Pre-Dose	24 Hours
2735 M	0	0	0	+	+	+
2736 M	0	0	0	1	+	+
2737 M	0	0	0	+	0	+
2738 M	0	0	0	0	0	+
2739 M	0	0	0	+	+,D	1
2740 M	0	0	0	+	0	+
2741 M	0	0	0	+	0	+
2742 M	0	0	0	1	+,D	+
2982 F	0	0	0	0	0	0
2983 F	0	0	0	1	+	3,Ed,N
2984 F	0	0	0	0	0	0
3162 F	0	0	0	0	0	0
2986 F	0	0	0	+	0	+
2987 F	0	0	0	+	+,D	1
2988 F	0	0	0	1	+	1

^aScored using the scale presented in Appendix B.

M=Male

F=Female

D=Desquamation

N=Necrosis

Ed=Edema

TABLE IB (cont.)

A CLOSED-PATCH REPEATED INSULT DERMAL SENSITIZATION STUDY IN
GUINEA PIGS

INDIVIDUAL DERMAL SCORES^a AT INDUCTION

GROUP: IVB INDUCTION MATERIAL: IPDI
CONCENTRATION: 90 mM

Animal No. and Sex	Induction 1		Induction 2		Induction 3	
	Pre-Dose	24 Hours	Pre-Dose	24 Hours	Pre-Dose	24 Hours
2720 M	0	0	0	2, Ed	+, D	2, Ed, D
2721 M	0	0	0	2, Ed	+, D	2, Ed
2722 M	0	0	0	2, Ed	+, D	2, Ed
2885 M	0	0	0	2, Ed	+	1, Ed
2724 M	0	0	0	+	+	1
2725 M	0	0	0	+	0	1, D
2726 M	0	0	0	1	+, D	1, D
2727 M	0	0	+	2, Ed	1	2, Ed
2966 F	0	0	0	0	0	1
2967 F	0	0	0	1, Ed	+, D	2, Ed
2968 F	0	0	0	+	0, D	1
3163 F	0	0	0	1	+, D	1
2970 F	0	0	0	1	1	2, Ed
2971 F	0	0	0	2, Ed	+, D	1
2972 F	0	0	+	1	+, D	1

^aScored using the scale presented in Appendix B.

M=Male
F=Female
D=Desquamation
Ed=Edema

TABLE IB (cont.)

A CLOSED-PATCH REPEATED INSULT DERMAL SENSITIZATION STUDY IN
GUINEA PIGS

INDIVIDUAL DERMAL SCORES^a AT INDUCTION

GROUP: IVC

INDUCTION MATERIAL: IPDI

CONCENTRATION: 300 mM

Animal No. and Sex	Induction 1		Induction 2		Induction 3	
	Pre-Dose	24 Hours	Pre-Dose	24 Hours	Pre-Dose	24 Hours
2728 M	0	0	0	2,Ed	1,D	2,Ed
2729 M	0	+	+	2,Ed	1,D	2,Ed
2730 M	0	+	0	2,Ed	+,D	2,Ed
2731 M	0	+,Ed	0,D	2,Ed	1,D	2,Ed
2732 M	0	+	+	2,Ed	+,D	2,Ed
2733 M	0	+	0	2,Ed	+,D	2,Ed
2734 M	0	+	0	2,Ed	+,D	2,Ed
2973 F	0	+	C,D	2,Ed	+,D	2,Ed
2974 F	0	+	0	2,Ed	+	1
2975 F	0	+	0	2,Ed	+,D	2
2976 F	0	1,Ed	1,D	2,Ed	1,D	3,Ed
2977 F	0	+	0	3,Ed	1,D	2,Ed
2978 F	0	0	0,D	3,Ed	1,D	3,Ed
2980 F	0	+	+,D	2,Ed	+	2
2981 F	0	+	0	2,Ed	+,D	3,Ed,N

^aScored using the scale presented in Appendix B.

M=Male

F=Female

D=Desquamation

Ed=Edema

N=Necrosis

Revised Page:

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Date:

4/9/85

TABLE IB (cont.)

A CLOSED-PATCH REPEATED INSULT DERMAL SENSITIZATION STUDY IN
GUINEA PIGS

INDIVIDUAL DERMAL SCORES^a AT INDUCTION

GROUP: VA

INDUCTION MATERIAL: m-TMXDI
CONCENTRATION: 10 mM

Animal No. and Sex	Induction 1		Induction 2		Induction 3	
	Pre-Dose	24 Hours	Pre-Dose	24 Hours	Pre-Dose	24 Hours
2830 M	0	0	0	0	0	+
2831 M	0	0	0	0	0	0
2832 M	0	0	0	0	0	0
2833 M	0	0	0	0	0	0
2834 M	0	0	0	0	0	+
2835 M	0	0	0	0	+	+
2836 M	0	0	0	0	0	+
2837 M	0	0	0	0	0	0
3077 F	0	0	0	+	0	0
3078 F	0	0	0	0	0	0
3079 F	0	0	0	0	0	0
3080 F	0	0	0	0	0	+
3081 F	0	0	0	0	0	0
3137 F	0	0	0	0	0	1
3083 F	0	0	0	0	0	0

^aScored using the scale presented in Appendix B.

M=Male
F=Female

TABLE IB (cont.)

A CLOSED-PATCH REPEATED INSULT DERMAL SENSITIZATION STUDY IN
GUINEA PIGS

INDIVIDUAL DERMAL SCORES^a AT INDUCTION

GROUP: VB INDUCTION MATERIAL: m-TMXDI
CONCENTRATION: 30 mM

Animal No. and Sex	Induction 1		Induction 2		Induction 3	
	Pre-Dose	24 Hours	Pre-Dose	24 Hours	Pre-Dose	24 Hours
2823 M	0	0	0	+	+	1
2824 M	0	0	0	+	0	+
2825 M	0	0	0	1	+	2
2826 M	0	0	0	0	0	1
2827 M	0	0	0	2	+,D	2
2828 M	0	0	0	1	+	2,Ed
2829 M	0	0	0	1	0,D	+
3069 F	0	0	0	1	+,D	2,Ed
3136 F	0	0	0	0	0	+
3071 F	0	0	0	+	0	+
3072 F	0	0	0	2	1,D	1,Ed
3073 F	0	0	0	0	0	1
3074 F	0	0	0	0	0	0
3075 F	0	0	0	+	+	1
3076 F	0	0	0	+	0	1

^aScored using the scale presented in Appendix B.

M=Male
F=Female
D=Desquamation
Ed=Edema

TABLE 1B (cont.)

A CLOSED-PATCH REPEATED INSULT DERMAL SENSITIZATION STUDY IN
GUINEA PIGS

INDIVIDUAL DERMAL SCORES^a AT INDUCTION

GROUP: VC

INDUCTION MATERIAL: m-TMXDI
CONCENTRATION: 100 mM

Animal No. and Sex	Induction 1		Induction 2		Induction 3	
	Pre-Dose	24 Hours	Pre-Dose	24 Hours	Pre-Dose	24 Hours
2814 M	0	0	0	2,Ed	1	3,Ed
2815 M	0	+	0	1	+	2,Ed
2816 M	0	+	+	2,Ed	1	2,Ed
2817 M	0	0	0	2,Ed	1,D	2,Ed
2818 M	0	0	0	1	1,D	2,Ed
2819 M	0	0	0	1	+,D	2,Ed
2821 M	0	+	0	2,Ed	1	2,Ed
2822 M	0	0	0	1,Ed	+,D	2,Ed
3062 F	0	0	0	1	+,D	2,Ed
3063 F	0	+	+	2,Ed	1	2,Ed
3064 F	0	+	0	2	+	3,Ed
3065 F	0	+	0	2,Ed	+	2,Ed
3066 F	0	0	0	1	+,D	2,Ed
3067 F	0	+	0	2,Ed	1	2,Ed
3068 F	0	0	0	1	+	1

^aScored using the scale presented in Appendix B.

M=Male

F=Female

D=Desquamation

Ed=Edema

TABLE IB (cont.)

A CLOSED-PATCH REPEATED INSULT DERMAL SENSITIZATION STUDY IN
GUINEA PIGS

INDIVIDUAL DERMAL SCORES^a AT INDUCTION

GROUP: VIA INDUCTION MATERIAL: HMDI
CONCENTRATION: 20 mM

Animal No. and Sex	Induction 1		Induction 2		Induction 3	
	Pre-Dose	24 Hours	Pre-Dose	24 Hours	Pre-Dose	24 Hours
2838 M	0	0	0	+	0	+
2839 M	0	0	0	0	0	0
2886 M	0	0	0	1	+	1
2841 M	0	0	0	+	+	+
2842 M	0	0	0	+	+,D	1
2887 M	0	0	0	0	0	0
2844 M	0	0	0	0	0	0
3084 F	0	0	0	0	0	0
3085 F	0	0	0	0	+	0
3086 F	0	0	0	0	+	1
3087 F	0	0	0	+	0	+
3131 F	0	0	0	0	0	0
3132 F	0	0	0	+	0	1
3138 F	0	0	0	0	0	0
3091 F	0	0	0	0	0	1

^aScored using the scale presented in Appendix B.

M=Male

F=Female

D=Desquamation

TABLE IB (cont.)

A CLOSED-PATCH REPEATED INSULT DERMAL SENSITIZATION STUDY IN
GUINEA PIGS

INDIVIDUAL DERMAL SCORES^a AT INDUCTION

GROUP: VIB INDUCTION MATERIAL: HMDI
CONCENTRATION: 60 mM

Animal No. and Sex	Induction 1		Induction 2		Induction 3	
	Pre-Dose	24 Hours	Pre-Dose	24 Hours	Pre-Dose	24 Hours
2845 M	0	0	+	1,Ed	+,D	1
2846 M	0	0	+	2,Ed	1,D	2,Ed
2847 M	0	0	0	+	0	0
2848 M	0	0	+	1	1,D	1
2849 M	0	0	0	1	+	2
2850 M	0	0	0	2	+,D	1
2852 M	0	0	+	1	+,D	2,Ed
2888 M	0	0	0	2	+,D	1
3092 F	0	0	0	1	0,D	2
3093 F	0	0	0	1	+,D	2,Ed
3094 F	0	0	0	2,Ed	+,D	2
3095 F	0	0	0	1	1,D	2,Ed
3096 F	0	0	0	+	0,D	1
3097 F	0	0	0	2,Ed	+,D	2,Ed
3098 F	0	0	0	1	0,D	1

^aScored using the scale presented in Appendix B.

M=Male

F=Female

D=Desquamation

Ed=Edema

TABLE IB (cont.)

A CLOSED-PATCH REPEATED INSULT DERMAL SENSITIZATION STUDY IN
GUINEA PIGS

INDIVIDUAL DERMAL SCORES^a AT INDUCTION

GROUP: VIC INDUCTION MATERIAL: HMDI
CONCENTRATION: 200 mM

Animal No. and Sex	Induction 1		Induction 2		Induction 3	
	Pre-Dose	24 Hours	Pre-Dose	24 Hours	Pre-Dose	24 Hours
2854 M	0	0	0	3,Ed	1	2,Ed
2855 M	0	0	+,D	2,Ed	1,D	2,Ed
2856 M	0	+	+,D	3,Ed	+,D	2,Ed
2857 M	0	0	0	2,Ed	+,D	2,Ed
2858 M	0	0	+	2,Ed	1,D	3,Ed,N
2859 M	0	+	0	2,Ed	+,D	2,Ed
2860 M	0	0	0	2,Ed	+,D	2,Ed
3099 F	0	0	0	3,Ed	+,D	3,Ed
3100 F	0	1	+,D	2,Ed	1,D	2,Ed
3101 F	0	+	+	2,Ed	+	3,Ed
3102 F	0	0	0	2,Ed	1	2,Ed
3103 F	0	0	+	2,Ed	+,D	2,Ed
3104 F	0	1	+,D	3,Ed	1,D	2,Ed
3105 F	0	+	0,D	3,Ed	1,D	3,Ed
3106 F	0	0	0	2	+,D	2

^aScored using the scale presented in Appendix B.

M=Male
F=Female
D=Desquamation
Ed=Edema
N=Necrosis

TABLE IB (cont.)

A CLOSED-PATCH REPEATED INSULT DERMAL SENSITIZATION STUDY IN
GUINEA PIGS

INDIVIDUAL DERMAL SCORES^a AT INDUCTION

GROUP: VIIA

INDUCTION MATERIAL: m-TMI
CONCENTRATION: 50 mM

Animal No. and Sex	Induction 1		Induction 2		Induction 3	
	Pre-Dose	24 Hours	Pre-Dose	24 Hours	Pre-Dose	24 Hours
2876 M	0	0	0	0	0	+
2878 M	0	0	0	0	0	2
2879 M	0	0	0	0	+	1
2880 M	0	0	0	0	0	1
2881 M	0	0	0	0	+,D	0
2882 M	0	0	0	0	0	0
2883 M	0	0	0	0	0	0
2884 M	0	0	0	0	0	0
3124 F	0	0	0	0	0	0
3125 F	0	0	0	0	0	+
3126 F	0	0	0	0	0	0
3127 F	0	0	0	0	0	+
3128 F	0	0	0	0	0	0
3129 F	0	0	0	0	0	0
3130 F	0	0	0	0	0	0

^aScored using the scale presented in Appendix B.

M=Male

F=Female

D=Desquamation

TABLE IB (cont.)

A CLOSED-PATCH REPEATED INSULT DERMAL SENSITIZATION STUDY IN
GUINEA PIGS

INDIVIDUAL DERMAL SCORES^a AT INDUCTION

GROUP: VIIB

INDUCTION MATERIAL: m-TMI
CONCENTRATION: 150 mM

Animal No. and Sex	Induction 1		Induction 2		Induction 3	
	Pre-Dose	24 Hours	Pre-Dose	24 Hours	Pre-Dose	24 Hours
2869 M	0	0	0	1	+,D	2,Ed
2870 M	0	0	0	+	0	1
2871 M	0	0	0	+	0	+
2872 M	0	0	0	1	+	2
2873 M	0	0	0	+	+,D	1
2874 M	0	0	0	2,Ed	+,D	3,Ed
2875 M	0	0	0	1	0,D	2
3115 F	0	0	0	1	0	1
3116 F	0	0	0	+	0	+
3117 F	0	0	0	1	+	1
3118 F	0	0	0	0	0	0
3119 F	0	0	0	1	0	1
3120 F	0	0	0	1,Ed	0,D	1
3121 F	0	0	0	0	0	2
3122 F	0	0	0	+	+	1

^aScored using the scale presented in Appendix B.

M=Male

F=Female

D=Desquamation

Ed=Edema

TABLE IB (cont.)

A CLOSED-PATCH REPEATED INSULT DERMAL SENSITIZATION STUDY IN
GUINEA PIGS

INDIVIDUAL DERMAL SCORES^a AT INDUCTION

GROUP: VIIC INDUCTION MATERIAL: m-TMI
CONCENTRATION: 500 mM

Animal No. and Sex	Induction 1		Induction 2		Induction 3	
	Pre-Dose	24 Hours	Pre-Dose	24 Hours	Pre-Dose	24 Hours
2861 M	0	<u>+</u>	<u>+</u>	2,Ed	2,D	3,Ed,N
2862 M	0	<u>+</u>	<u>+</u>	2,Ed	3,Ed,N,D ^b	2,Ed
2863 M	0	<u>+</u>	<u>+</u> ,D	3,Ed	2,D	3,Ed
2864 M	0	<u>+</u>	<u>+</u>	3,Ed	1,D	3,Ed,N
2865 M	0	1,Ed	<u>+</u> ,D	2,Ed	1,D	3,Ed
2866 M	0	0	<u>+</u>	2,Ed	1,D	3,Ed
2867 M	0	0	<u>+</u> ,D	2,Ed	2,D	3,Ed
2868 M	0	<u>+</u>	1,D	2,Ed	1,D	3,Ed,N
3107 F	0	<u>+</u>	1,D	2,Ed	1,D	3,Ed
3108 F	0	<u>+</u> ,Ed	1,D	2,Ed	1,D	3,Ed,N
3110 F	0	<u>+</u>	<u>+</u> ,D	2,Ed	1,D	3,Ed
3111 F	0	<u>+</u>	<u>+</u> ,D	2,Ed	<u>+</u> ,D	2,Ed
3112 F	0	<u>+</u>	0,D	2,Ed	1,D	3,Ed,N
3113 F	0	<u>+</u>	2,D	2,Ed	1,D ^c	3,Ed,N
3114 F	0	0	1,Ed,D	2,Ed	1,D	3,Ed,N

^aScored using the scale presented in Appendix B.

^bBecause of tissue damage (necrosis) the patch for the third induction was placed at a new site (over undamaged skin).

^cFoci of necrosis at edge of dose site.

M=Male

F=Female

D=Desquamation

Ed=Edema

N=Necrosis

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TABLE IIA

A CLOSED-PATCH REPEATED INSULT DERMAL SENSITIZATION STUDY IN
GUINEA PIGS

INCIDENCE OF DERMAL RESPONSE AT CHALLENGE

Material	Induction Concentration (mM)	No. of Animals ^a with scores Greater than 0					No. of Animals ^a with scores Greater than +				
		Challenge Concentration					Challenge Concentration				
		Low	Low-Mid	Mid-High	High	High	Low	Low-Mid	Mid-High	High	High
TDI	30	-	-	-	-	2	-	-	-	-	-
	90	-	-	-	-	8	-	-	-	-	2
	300	-	-	-	2	7	-	-	-	-	3
MDI	10	-	-	1	3	4	-	-	-	1	-
	30	-	-	-	-	5	-	-	-	-	-
	100	-	-	-	-	2	-	-	-	-	-
p-TMXDI	20	-	1	2	10	14	-	-	-	1	9
	60	-	-	-	9	14	-	-	-	1	11
	200	-	-	1	9	15	-	-	-	3	13
IPDI	30	-	-	-	1	10	-	-	-	-	3
	90	-	-	-	4	12	-	-	-	-	4
	300	-	-	-	5	14	-	-	-	1	10
m-TMXDI	10	1	-	-	3	11	-	-	-	-	3
	30	-	-	1	7	11	-	-	-	2	6
	100	-	-	2	9	15	-	-	1	3	10
HMDI	20	-	-	-	1	9 ^b	-	-	-	-	2
	60	-	-	-	5	13 ^b	-	-	-	-	6
	200	-	-	-	5	15 ^b	-	-	-	1	13
m-TMI	50	-	-	1	5	11	-	-	-	1	6
	150	-	-	-	4	15	-	-	-	-	6
	500	-	-	4	12	15	-	-	1	6	15

^aN=15 Per Group. Numbers represent animals with indicated score at 24 and/or 48 hours. When scores differed at 24 hours the highest score was used.

Irritation control animals had scores of 0 unless indicated otherwise.

^bHMDI - 2 of 6 irritation controls at high dose had scores of + at 48 hours only.

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TABLE IIB

A CLOSED-PATCH REPEATED INSULT DERMAL SENSITIZATION STUDY IN
GUINEA PIGS

SUMMARY OF RESPONSES TO CHALLENGE^a

MATERIAL: TDI

Group	Induction Concentration (milliMolar)	Challenge Concentration (milliMolar)	Score: Hr:	0	+	1	2	3	Edema
IA	30	0.09	24	15	-	-	-	-	-
			48	15	-	-	-	-	-
		0.9	24	15	-	-	-	-	-
			48	15	-	-	-	-	-
		9.0	24	15	-	-	-	-	-
			48	15	-	-	-	-	-
		30	24	15	-	-	-	-	-
			48	15	-	-	-	-	-
		90	24	13	2	-	-	-	-
			48	15	-	-	-	-	-
IB	90	0.09	24	15	-	-	-	-	-
			48	15	-	-	-	-	-
		0.9	24	15	-	-	-	-	-
			48	15	-	-	-	-	-
		9.0	24	15	-	-	-	-	-
			48	15	-	-	-	-	-
		30	24	15	-	-	-	-	-
			48	15	-	-	-	-	-
		90	24	7	6	2	-	-	-
			48	9	6	-	-	-	-
IC	300	0.09	24	15	-	-	-	-	-
			48	15	-	-	-	-	-
		0.9	24	15	-	-	-	-	-
			48	15	-	-	-	-	-
		9.0	24	15	-	-	-	-	-
			48	15	-	-	-	-	-
		30	24	13	2	-	-	-	-
			48	15	-	-	-	-	-
		90	24	8	4	3	-	-	-
			48	11	3	1	-	-	-
ID (Irritation Control)	None	0.09	24	6	-	-	-	-	-
			48	6	-	-	-	-	-
		0.9	24	6	-	-	-	-	-
			48	6	-	-	-	-	-
		9.0	24	6	-	-	-	-	-
			48	6	-	-	-	-	-
		30	24	6	-	-	-	-	-
			48	6	-	-	-	-	-
		90	24	6	-	-	-	-	-
			48	6	-	-	-	-	-

^aNumbers presented are numbers of animals with indicated score. See
Appendix B for scoring system. N=15 per group.

TABLE IIB (cont.)

A CLOSED-PATCH REPEATED INSULT DERMAL SENSITIZATION STUDY IN
GUINEA PIGS

SUMMARY OF RESPONSES TO CHALLENGE^a

MATERIAL: MDI

Group	Induction Concentration (milliMolar)	Challenge Concentration (milliMolar)	Score: Hr:	0	+	1	2	3	Edema
IIA	10	0.03	24	15	-	-	-	-	-
			48	15	-	-	-	-	-
		0.3	24	15	-	-	-	-	-
			48	15	-	-	-	-	-
		3	24	14	1	-	-	-	-
			48	14	1	-	-	-	-
		10	24	14	-	1	-	-	-
			48	12	3	-	-	-	-
		30	24	12	3	-	-	-	-
			48	11	4	-	-	-	-
IIB	30	0.03	24	15	-	-	-	-	-
			48	15	-	-	-	-	-
		0.3	24	15	-	-	-	-	-
			48	15	-	-	-	-	-
		3	24	15	-	-	-	-	-
			48	15	-	-	-	-	-
		10	24	15	-	-	-	-	-
			48	15	-	-	-	-	-
		30	24	12	3	-	-	-	-
			48	11	4	-	-	-	-
IIC	100	0.03	24	15	-	-	-	-	-
			48	15	-	-	-	-	-
		0.3	24	15	-	-	-	-	-
			48	15	-	-	-	-	-
		3	24	15	-	-	-	-	-
			48	15	-	-	-	-	-
		10	24	15	-	-	-	-	-
			48	15	-	-	-	-	-
		30	24	13	2	-	-	-	-
			48	14	1	-	-	-	-
IID (Irritation Control)	None	0.03	24	6	-	-	-	-	-
			48	6	-	-	-	-	-
		0.3	24	6	-	-	-	-	-
			48	6	-	-	-	-	-
		3	24	6	-	-	-	-	-
			48	6	-	-	-	-	-
		10	24	6	-	-	-	-	-
			48	6	-	-	-	-	-
		30	24	6	-	-	-	-	-
			48	6	-	-	-	-	-

^aNumbers presented are numbers of animals with indicated score. See Appendix B for scoring system. N=15 per group.

TABLE IIB (cont.)

A CLOSED-PATCH REPEATED INSULT DERMAL SENSITIZATION STUDY IN
GUINEA PIGS

SUMMARY OF RESPONSES TO CHALLENGE^a

MATERIAL: p-TMXDI

Group	Induction Concentration (milliMolar)	Challenge Concentration (milliMolar)	Score: Hr:	0	+	1	2	3	Edema
IIIA	20	0.06	24	15	-	-	-	-	-
			48	15	-	-	-	-	-
		0.6	24	14	1	-	-	-	-
			48	15	-	-	-	-	-
		6	24	13	2	-	-	-	-
			48	13	2	-	-	-	-
		20	24	7	7	1	-	-	-
			48	8	6	1	-	-	-
		60	24	2	5	6	2	-	-
			48	1	8	6	-	-	-
IIIB	60	0.06	24	15	-	-	-	-	-
			48	15	-	-	-	-	-
		0.6	24	15	-	-	-	-	-
			48	15	-	-	-	-	-
		6	24	15	-	-	-	-	-
			48	15	-	-	-	-	-
		20	24	6	8	1	-	-	-
			48	13	2	-	-	-	-
		60	24	1	4	9	1	-	-
			48	2	10	3	-	-	-
IIIC	200	0.06	24	15	-	-	-	-	-
			48	15	-	-	-	-	-
		0.6	24	15	-	-	-	-	-
			48	15	-	-	-	-	-
		6	24	14	1	-	-	-	-
			48	14	1	-	-	-	-
		20	24	6	6	3	-	-	-
			48	8	6	1	-	-	-
		60	24	-	2	9	4	-	3
			48	-	6	8	1	-	-
IIID (Irritation Control)	None	0.06	24	6	-	-	-	-	-
			48	6	-	-	-	-	-
		0.6	24	6	-	-	-	-	-
			48	6	-	-	-	-	-
		6	24	6	-	-	-	-	-
			48	6	-	-	-	-	-
		20	24	6	-	-	-	-	-
			48	6	-	-	-	-	-
		60	24	6	-	-	-	-	-
			48	6	-	-	-	-	-

^aNumbers presented are numbers of animals with indicated score. See
Appendix B for scoring system. N=15 per group.

TABLE IIB (cont.)

A CLOSED-PATCH REPEATED INSULT DERMAL SENSITIZATION STUDY IN
GUINEA PIGS

SUMMARY OF RESPONSES TO CHALLENGE^a

MATERIAL: IPDI

Group	Induction Concentration (milliMolar)	Challenge Concentration (milliMolar)	Score: Hr:	0	+	1	2	3	Edema
IVA	30	0.09	24	15	-	-	-	-	-
			48	15	-	-	-	-	-
		0.9	24	15	-	-	-	-	-
			48	15	-	-	-	-	-
		9	24	15	-	-	-	-	-
			48	15	-	-	-	-	-
		30	24	14	1	-	-	-	-
			48	14	1	-	-	-	-
		90	24	6	7	1	1	-	-
			48	6	7	2	-	-	-
IVB	90	0.09	24	15	-	-	-	-	-
			48	15	-	-	-	-	-
		0.9	24	15	-	-	-	-	-
			48	15	-	-	-	-	-
		9	24	15	-	-	-	-	-
			48	15	-	-	-	-	-
		30	24	12	3	-	-	-	-
			48	12	3	-	-	-	-
		90	24	3	9	3	-	-	-
			48	4	9	2	-	-	-
IVC	300	0.09	24	15	-	-	-	-	-
			48	15	-	-	-	-	-
		0.9	24	15	-	-	-	-	-
			48	15	-	-	-	-	-
		9	24	15	-	-	-	-	-
			48	15	-	-	-	-	-
		30	24	11	3	1	-	-	-
			48	12	3	-	-	-	-
		90	24	1	4	7	3	-	1
			48	4	7	4	-	-	-
IVD (Irritation Control)	None	0.09	24	6	-	-	-	-	-
			48	6	-	-	-	-	-
		0.9	24	6	-	-	-	-	-
			48	6	-	-	-	-	-
		9	24	6	-	-	-	-	-
			48	6	-	-	-	-	-
		30	24	6	-	-	-	-	-
			48	6	-	-	-	-	-
		90	24	6	-	-	-	-	-
			48	6	-	-	-	-	-

^aNumbers presented are numbers of animals with indicated score. See Appendix B for scoring system. N=15 per group.

TABLE IIB (cont.)

A CLOSED-PATCH REPEATED INSULT DERMAL SENSITIZATION STUDY IN
GUINEA PIGS

SUMMARY OF RESPONSES TO CHALLENGE^a

MATERIAL: m-TMXDI

Group	Induction Concentration (milliMolar)	Challenge Concentration (milliMolar)	Score: Hr:	0	+	1	2	3	Edema
VA	10	0.03	24	14	1	-	-	-	-
			48	14	1	-	-	-	-
		0.3	24	15	-	-	-	-	-
			48	15	-	-	-	-	-
		3	24	15	-	-	-	-	-
			48	15	-	-	-	-	-
		10	24	12	3	-	-	-	-
			48	13	2	-	-	-	-
		30	24	5	9	1	-	-	-
			48	4	8	3	-	-	-
VB	30	0.03	24	15	-	-	-	-	-
			48	15	-	-	-	-	-
		0.3	24	15	-	-	-	-	-
			48	15	-	-	-	-	-
		3	24	14	1	-	-	-	-
			48	14	1	-	-	-	-
		10	24	9	4	2	-	-	-
			48	10	4	1	-	-	-
		30	24	4	5	5	1	-	-
			48	4	6	5	-	-	-
VC	100	0.03	24	15	-	-	-	-	-
			48	15	-	-	-	-	-
		0.3	24	15	-	-	-	-	-
			48	15	-	-	-	-	-
		3	24	13	1	1	-	-	-
			48	14	-	1	-	-	-
		10	24	7	5	2	1	-	-
			48	8	5	2	-	-	-
		30	24	-	5	7	3	-	-
			48	1	8	5	1	-	-
VD (Irritation Control)	None	0.03	24	6	-	-	-	-	-
			48	6	-	-	-	-	-
		0.3	24	6	-	-	-	-	-
			48	6	-	-	-	-	-
		3	24	6	-	-	-	-	-
			48	6	-	-	-	-	-
		10	24	6	-	-	-	-	-
			48	6	-	-	-	-	-
		30	24	6	-	-	-	-	-
			48	6	-	-	-	-	-

^aNumbers presented are numbers of animals with indicated score. See Appendix B for scoring system. N=15 per group.

TABLE IIB (cont.)

A CLOSED-PATCH REPEATED INSULT DERMAL SENSITIZATION STUDY IN
GUINEA PIGS

SUMMARY OF RESPONSES TO CHALLENGE^a

MATERIAL: HMDI

Group	Induction Concentration (milliMolar)	Challenge Concentration (milliMolar)	Score: Hr:	0	+	1	2	3	Edema
				—	—	—	—	—	—
VIA	20	0.06	24	15	-	-	-	-	-
			48	15	-	-	-	-	-
		0.6	24	15	-	-	-	-	-
			48	15	-	-	-	-	-
		6	24	15	-	-	-	-	-
			48	15	-	-	-	-	-
	20		24	14	1	-	-	-	-
			48	14	1	-	-	-	-
	60		24	6	8	1	-	-	-
			48	6	7	2	-	-	-
VIB	60	0.06	24	15	-	-	-	-	-
			48	15	-	-	-	-	-
		0.6	24	15	-	-	-	-	-
			48	15	-	-	-	-	-
		6	24	15	-	-	-	-	-
			48	15	-	-	-	-	-
	20		24	10	5	-	-	-	-
			48	13	2	-	-	-	-
	60		24	3	6	6	-	-	1
			48	2	11	2	-	-	-
VIC	200	0.06	24	15	-	-	-	-	-
			48	15	-	-	-	-	-
		0.6	24	15	-	-	-	-	-
			48	15	-	-	-	-	-
		6	24	15	-	-	-	-	-
			48	15	-	-	-	-	-
	20		24	10	4	1	-	-	-
			48	10	5	-	-	-	-
	60		24	1	2	8	4	-	4
			48	-	7	8	-	-	-
VID (Irritation Control)	None	0.06	24	6	-	-	-	-	-
			48	6	-	-	-	-	-
		0.6	24	6	-	-	-	-	-
			48	6	-	-	-	-	-
		6	24	6	-	-	-	-	-
			48	6	-	-	-	-	-
	20		24	6	-	-	-	-	-
			48	6	-	-	-	-	-
	60		24	6	-	-	-	-	-
			48	4	2	-	-	-	-

^aNumbers presented are numbers of animals with indicated score. See
Appendix B for scoring system. N=15 per group.

TABLE IIB (cont.)

A CLOSED-PATCH REPEATED INSULT DERMAL SENSITIZATION STUDY IN
GUINEA PIGS

SUMMARY OF RESPONSES TO CHALLENGE^a

MATERIAL: m-TMI

Group	Induction Concentration (milliMolar)	Challenge Concentration (milliMolar)	Score: Hr:	0	+	1	2	3	Edema
VIIA	50	0.15	24	15	-	-	-	-	-
			48	15	-	-	-	-	-
		1.5	24	15	-	-	-	-	-
			48	15	-	-	-	-	-
		15	24	15	-	-	-	-	-
			48	14	1	-	-	-	-
		50	24	11	4	-	-	-	-
			48	10	4	1	-	-	-
		150	24	6	3	6	-	-	1
			48	5	4	6	-	-	1
VIIB	150	0.15	24	15	-	-	-	-	-
			48	15	-	-	-	-	-
		1.5	24	15	-	-	-	-	-
			48	15	-	-	-	-	-
		15	24	15	-	-	-	-	-
			48	15	-	-	-	-	-
		50	24	12	3	-	-	-	-
			48	14	1	-	-	-	-
		150	24	1	8	6	-	-	1
			48	-	12	3	-	-	-
VIIC	500	0.15	24	15	-	-	-	-	-
			48	15	-	-	-	-	-
		1.5	24	15	-	-	-	-	-
			48	15	-	-	-	-	-
		15	24	11	3	-	1	-	-
			48	13	1	1	-	-	-
		50	24	4	5	4	1	1	2
			48	3	8	3	1	-	2
		150	24	-	-	6	7	2	8
			48	-	2	9	4	-	2
VIID (Irritation Control)	None	0.15	24	6	-	-	-	-	-
			48	6	-	-	-	-	-
		1.5	24	6	-	-	-	-	-
			48	6	-	-	-	-	-
		15	24	6	-	-	-	-	-
			48	6	-	-	-	-	-
		50	24	6	-	-	-	-	-
			48	6	-	-	-	-	-
		150	24	6	-	-	-	-	-
			48	6	-	-	-	-	-

^aNumbers presented are number of animals with indicated score. See Appendix B for scoring system. N=15 per group.

TABLE IIC

A CLOSED-PATCH REPEATED INSULT DERMAL SENSITIZATION STUDY IN
GUINEA PIGS

INDIVIDUAL DERMAL SCORES AT CHALLENGE^a

GROUP: IA

INDUCTION MATERIAL: TDI
CONCENTRATION: 30 mM

Animal No. and Sex	Interval (Hr):	Challenge Concentration (mM):									
		90		30		9.0		0.9		0.09	
		24	48	24	48	24	48	24	48	24	48
2750 M		0	0	0	0	0	0	0	0	0	0
2751 M		0	0	0	0	0	0	0	0	0	0
2753 M		+	0	0	0	0	0	0	0	0	0
2754 M		0	0	0	0	0	0	0	0	0	0
2755 M		0	0	0	0	0	0	0	0	0	0
2756 M		+	0	0	0	0	0	0	0	0	0
2757 M		0	0	0	0	0	0	0	0	0	0
2758 M		0	0	0	0	0	0	0	0	0	0
2998 F		0	0	0	0	0	0	0	0	0	0
2999 F		0	0	0	0	0	0	0	0	0	0
3164 F		0	0	0	0	0	0	0	0	0	0
3002 F		0	0	0	0	0	0	0	0	0	0
3003 F		0	0	0	0	0	0	0	0	0	0
3004 F		0	0	0	0	0	0	0	0	0	0
3006 F		0	0	0	0	0	0	0	0	0	0

^aScored using the scale presented in Appendix B.

M=Male

F=Female

TABLE IIC (cont.)

A CLOSED-PATCH REPEATED INSULT DERMAL SENSITIZATION STUDY IN
GUINEA PIGS

INDIVIDUAL DERMAL SCORES AT CHALLENGE^a

GROUP: IB INDUCTION MATERIAL: TDI
CONCENTRATION: 90 mM

Animal No. and Sex	Interval (Hr):	Challenge Concentration (mM):									
		90		30		9.0		0.9		0.09	
		24	48	24	48	24	48	24	48	24	48
2799 M		0	0	0	0	0	0	0	0	0	0
2800 M		+	0	0	0	0	0	0	0	0	0
2801 M		+	+	0	0	0	0	0	0	0	0
2802 M		1	+	0	0	0	0	0	0	0	0
2803 M		0	0	0	0	0	0	0	0	0	0
2804 M		1	+	0	0	0	0	0	0	0	0
2805 M		0	0	0	0	0	0	0	0	0	0
2806 M		0	0	0	0	0	0	0	0	0	0
3047 F		0	0	0	0	0	0	0	0	0	0
3048 F		0	0	0	0	0	0	0	0	0	0
3049 F		+	+	0	0	0	0	0	0	0	0
3050 F		0	0	0	0	0	0	0	0	0	0
3051 F		+	+	0	0	0	0	0	0	0	0
3052 F		+	+	0	0	0	0	0	0	0	0
3053 F		+	0	0	0	0	0	0	0	0	0

^aScored using the scale presented in Appendix B.
M=Male
F=Female

TABLE IIC (cont.)

A CLOSED-PATCH REPEATED INSULT DERMAL SENSITIZATION STUDY IN
GUINEA PIGS

INDIVIDUAL DERMAL SCORES AT CHALLENGE^a

GROUP: IC

INDUCTION MATERIAL: TDI

CONCENTRATION: 300 mM

Animal No. and Sex	Interval (Hr):	Challenge Concentration (mM):									
		90		30		9.0		0.9		0.09	
		24	48	24	48	24	48	24	48	24	48
2807 M		0	0	0	0	0	0	0	0	0	0
2808 M		0	0	0	0	0	0	0	0	0	0
2809 M		1	+	0	0	0	0	0	0	0	0
2810 M		+	+	0	0	0	0	0	0	0	0
2811 M		0	0	0	0	0	0	0	0	0	0
2812 M		0	0	0	0	0	0	0	0	0	0
2813 M		+	0	0	0	0	0	0	0	0	0
3054 F		0	0	0	0	0	0	0	0	0	0
3055 F		0	0	0	0	0	0	0	0	0	0
3056 F		0	0	0	0	0	0	0	0	0	0
3134 F		+	0	0	0	0	0	0	0	0	0
3058 F		+	0	0	0	0	0	0	0	0	0
3059 F		1	+	+	0	0	0	0	0	0	0
3060 F		1	1	+	0	0	0	0	0	0	0
3061 F		0	0	0	0	0	0	0	0	0	0

^aScored using the scale presented in Appendix B.

M=Male

F=Female

TABLE IIC (cont.)

A CLOSED-PATCH REPEATED INSULT DERMAL SENSITIZATION STUDY IN
GUINEA PIGS

INDIVIDUAL DERMAL SCORES AT CHALLENGE^a

GROUP: ID

INDUCTION MATERIAL: None (Irritation controls)
CHALLENGE MATERIAL: TDI

Animal No. and Sex	Interval (Hr):	Challenge Concentration (mM):									
		90		30		9.0		0.9		0.09	
		24	48	24	48	24	48	24	48	24	48
2892 M		0	0	0	0	0	0	0	0	0	0
2893 M		0	0	0	0	0	0	0	0	0	0
2894 M		0	0	0	0	0	0	0	0	0	0
3143 F		0	0	0	0	0	0	0	0	0	0
3144 F		0	0	0	0	0	0	0	0	0	0
3145 F		0	0	0	0	0	0	0	0	0	0

^aScored using the scale presented in Appendix B.

M=Male

F=Female

TABLE IIC (cont.)

A CLOSED-PATCH REPEATED INSULT DERMAL SENSITIZATION STUDY IN
GUINEA PIGSINDIVIDUAL DERMAL SCORES AT CHALLENGE^a

GROUP: IIA

INDUCTION MATERIAL: MDI

CONCENTRATION: 10 mM

Animal No. and Sex	Interval (Hr):	Challenge Concentration (mM):									
		30		10		3.0		0.3		0.03	
		24	48	24	48	24	48	24	48	24	48
2759 M		0	0	0	0	0	0	0	0	0	0
2760 M		0	0	0	0	0	0	0	0	0	0
2762 M		0	+	0	+	0	0	0	0	0	0
2763 M		+	+	1	+	+	+	0	0	0	0
2764 M		0	0	0	0	0	0	0	0	0	0
2765 M		0	0	0	0	0	0	0	0	0	0
2766 M		0	0	0	0	0	0	0	0	0	0
3007 F		+	+	0	+	0	0	0	0	0	0
3008 F		0	0	0	0	0	0	0	0	0	0
3009 F		0	0	0	0	0	0	0	0	0	0
3010 F		0	0	0	0	0	0	0	0	0	0
3011 F		+	+	0	0	0	0	0	0	0	0
3012 F		0	0	0	0	0	0	0	0	0	0
3013 F		0	0	0	0	0	0	0	0	0	0
3014 F		0	0	0	0	0	0	0	0	0	0

^aScored using the scale presented in Appendix B.

M=Male

F=Female

TABLE IIC (cont.)

A CLOSED-PATCH REPEATED INSULT DERMAL SENSITIZATION STUDY IN
GUINEA PIGS

INDIVIDUAL DERMAL SCORES AT CHALLENGE^a

GROUP: IIB

INDUCTION MATERIAL: MDI
CONCENTRATION: 30 mM

Animal No. and Sex	Interval (Hr):	Challenge Concentration (mM):									
		30		10		3.0		0.3		0.03	
		24	48	24	48	24	48	24	48	24	48
2767 M		+	+	0	0	0	0	0	0	0	0
2768 M		0	0	0	0	0	0	0	0	0	0
2769 M		0	+	0	0	0	0	0	0	0	0
2770 M		0	0	0	0	0	0	0	0	0	0
2771 M		0	0	0	0	0	0	0	0	0	0
2772 M		0	0	0	0	0	0	0	0	0	0
2773 M		0	0	0	0	0	0	0	0	0	0
2774 M		0	0	0	0	0	0	0	0	0	0
3015 F		+	0	0	0	0	0	0	0	0	0
3016 F		0	0	0	0	0	0	0	0	0	0
3017 F		0	+	0	0	0	0	0	0	0	0
3018 F		0	0	0	0	0	0	0	0	0	0
3019 F		0	0	0	0	0	0	0	0	0	0
3020 F		0	0	0	0	0	0	0	0	0	0
3021 F		+	+	0	0	0	0	0	0	0	0

^aScored using the scale presented in Appendix B.
M=Male
F=Female

TABLE IIC (cont.)

A CLOSED-PATCH REPEATED INSULT DERMAL SENSITIZATION STUDY IN
GUINEA PIGS

INDIVIDUAL DERMAL SCORES AT CHALLENGE^a

GROUP: IIC

INDUCTION MATERIAL: MDI

CONCENTRATION: 100 mM

Animal No. and Sex	Interval (Hr):	Challenge Concentration (mM):									
		30		10		3.0		0.3		0.03	
		24	48	24	48	24	48	24	48	24	48
2775 M		+	0	0	0	0	0	0	0	0	0
2776 M		0	0	0	0	0	0	0	0	0	0
2777 M		0	0	0	0	0	0	0	0	0	0
2778 M		0	0	0	0	0	0	0	0	0	0
2779 M		0	0	0	0	0	0	0	0	0	0
2780 M		0	0	0	0	0	0	0	0	0	0
2781 M		0	0	0	0	0	0	0	0	0	0
3022 F		0	0	0	0	0	0	0	0	0	0
3023 F		0	0	0	0	0	0	0	0	0	0
3135 F		0	0	0	0	0	0	0	0	0	0
3025 F		0	0	0	0	0	0	0	0	0	0
3026 F		+	+	0	0	0	0	0	0	0	0
3027 F		0	0	0	0	0	0	0	0	0	0
3028 F		0	0	0	0	0	0	0	0	0	0
3029 F		0	0	0	0	0	0	0	0	0	0

^aScored using the scale presented in Appendix B.

M=Male

F=Female

TABLE IIC (cont.)

A CLOSED-PATCH REPEATED INSULT DERMAL SENSITIZATION STUDY IN
GUINEA PIGS

INDIVIDUAL DERMAL SCORES AT CHALLENGE^a

GROUP: IID

INDUCTION MATERIAL: None (Irritation Control)

CHALLENGE MATERIAL: MDI

Animal No. and Sex	Interval (Hr):	Challenge Concentration (mM):									
		30		10		3.0		0.3		0.03	
		24	48	24	48	24	48	24	48	24	48
2895 M		0	0	0	0	0	0	0	0	0	0
2896 M		0	0	0	0	0	0	0	0	0	0
2897 M		0	0	0	0	0	0	0	0	0	0
3146 F		0	0	0	0	0	0	0	0	0	0
3147 F		0	0	0	0	0	0	0	0	0	0
3148 F		0	0	0	0	0	0	0	0	0	0

^aScored using the scale presented in Appendix B.

M=Male

F=Female

TABLE IIC (cont.)

A CLOSED-PATCH REPEATED INSULT DERMAL SENSITIZATION STUDY IN
GUINEA PIGS

INDIVIDUAL DERMAL SCORES AT CHALLENGE^a

GROUP: IIIA

INDUCTION MATERIAL: p-TMXDI
CONCENTRATION: 20 mM

Animal No. and Sex	Interval (Hr):	Challenge Concentration (mM):									
		60		20		6.0		0.6		0.06	
		24	48	24	48	24	48	24	48	24	48
2743 M		1	1	+	0	0	0	0	0	0	0
2744 M		0	0	0	0	0	0	0	0	0	0
2745 M		1	+	+	0	0	0	0	0	0	0
2746 M		1	+	+	+	0	0	0	0	0	0
2747 M		+	1	+	+	0	0	0	0	0	0
2748 M		+	+	+	0	0	0	0	0	0	0
2749 M		1	+	0	0	0	0	0	0	0	0
2989 F		2	1	+	+	0	0	0	0	0	0
2990 F		2	1	1	1	+	+	0	0	0	0
2991 F		+	+	0	0	0	0	0	0	0	0
2992 F		1	1	0	+	0	0	0	0	0	0
2993 F		+	+	0	0	0	0	0	0	0	0
2994 F		1	1	+	+	+	+	+	0	0	0
2995 F		+	+	0	0	0	0	0	0	0	0
2997 F		0	+	0	+	0	0	0	0	0	0

^aScored using the scale presented in Appendix B.
M=Male
F=Female

TABLE IIC (cont.)

A CLOSED-PATCH REPEATED INSULT DERMAL SENSITIZATION STUDY IN
GUINEA PIGS

INDIVIDUAL DERMAL SCORES AT CHALLENGE^a

GROUP: IIIB

INDUCTION MATERIAL: p-TMXDI
CONCENTRATION: 60 mM

Animal No. and Sex	Interval (hr):	Challenge Concentration (mM):									
		60		20		6.0		0.6		0.06	
		24	48	24	48	24	48	24	48	24	48
2782 M		1	+	0	0	0	0	0	0	0	0
2783 M		0	0	0	0	0	0	0	0	0	0
2784 M		1	+	+	0	0	0	0	0	0	0
2785 M		+	+	0	0	0	0	0	0	0	0
2788 M		+	0	+	0	0	0	0	0	0	0
2789 M		1	+	+	0	0	0	0	0	0	0
2790 M		1	1	+	0	0	0	0	0	0	0
2791 M		+	+	0	0	0	0	0	0	0	0
3030 F		2	1	1	+	0	0	0	0	0	0
3031 F		1	+	+	0	0	0	0	0	0	0
3033 F		1	+	0	0	0	0	0	0	0	0
3034 F		1	+	+	0	0	0	0	0	0	0
3035 F		1	+	+	0	0	0	0	0	0	0
3036 F		1	+	+	+	0	0	0	0	0	0
3037 F		+	1	0	0	0	0	0	0	0	0

^aScored using the scale presented in Appendix B.

M=Male

F=Female

TABLE IIC (cont.)

A CLOSED-PATCH REPEATED INSULT DERMAL SENSITIZATION STUDY IN
GUINEA PIGS

INDIVIDUAL DERMAL SCORES AT CHALLENGE^a

GROUP: IIIC

INDUCTION MATERIAL: p-TMXDI
CONCENTRATION: 200 mM

Animal No. and Sex	Interval (Hr):	Challenge Concentration (mM):									
		60		20		6.0		0.6		0.06	
		24	48	24	48	24	48	24	48	24	48
2792 M		2,Ed	2	1	1	+	+	0	0	0	0
2793 M		1	1	1	+	0	0	0	0	0	0
2794 M		2,Ed	1	1	+	0	0	0	0	0	0
2795 M		1,Ed	1	+	+	0	0	0	0	0	0
2796 M		2	1	+	+	0	0	0	0	0	0
2797 M		1	+	0	0	0	0	0	0	0	0
2798 M		1	1	0	0	0	0	0	0	0	0
3038 F		1	+	0	0	0	0	0	0	0	0
3039 F		1	+	+	0	0	0	0	0	0	0
3040 F		2	1	+	0	0	0	0	0	0	0
3041 F		+	+	0	0	0	0	0	0	0	0
3042 F		1	1	+	+	0	0	0	0	0	0
3044 F		1	+	0	0	0	0	0	0	0	0
3045 F		1	1	+	+	0	0	0	0	0	0
3046 F		+	+	0	0	0	0	0	0	0	0

^aScored using the scale presented in Appendix B.

M=Male

F=Female

Ed=Edema

TABLE IIC (cont.)

A CLOSED-PATCH REPEATED INSULT DERMAL SENSITIZATION STUDY IN
GUINEA PIGS

INDIVIDUAL DERMAL SCORES AT CHALLENGE^a

GROUP: IIID

INDUCTION MATERIAL: None (Irritation Control)
CHALLENGE MATERIAL: p-TMXDI

Animal No. and Sex	Interval (Hr):	Challenge Concentration (mM):									
		60		20		6.0		0.6		0.06	
		24	48	24	48	24	48	24	48	24	48
2898 M		0	0	0	0	0	0	0	0	0	0
2919 M		0	0	0	0	0	0	0	0	0	0
2900 M		0	0	0	0	0	0	0	0	0	0
3149 F		0	0	0	0	0	0	0	0	0	0
3150 F		0	0	0	0	0	0	0	0	0	0
3151 F		0	0	0	0	0	0	0	0	0	0

^aScored using the scale presented in Appendix B.

M=Male

F=Female

TABLE IIC (cont.)

A CLOSED-PATCH REPEATED INSULT DERMAL SENSITIZATION STUDY IN
GUINEA PIGS

INDIVIDUAL DERMAL SCORES AT CHALLENGE^a

GROUP: IVA

INDUCTION MATERIAL: IPDI
CONCENTRATION: 30 mM

Animal No. and Sex	Interval (Hr):	Challenge Concentration (mM):									
		90		30		9.0		0.9		0.09	
		24	48	24	48	24	48	24	48	24	48
2735 M		0	0	0	0	0	0	0	0	0	0
2736 M		+	+	0	0	0	0	0	0	0	0
2737 M		+	+	0	0	0	0	0	0	0	0
2738 M		0	+	0	0	0	0	0	0	0	0
2739 M		+	0	0	0	0	0	0	0	0	0
2740 M		0	0	0	0	0	0	0	0	0	0
2741 M		+	+	0	0	0	0	0	0	0	0
2742 M		0	0	0	0	0	0	0	0	0	0
2982 F		0	0	0	0	0	0	0	0	0	0
2983 F		2	1	+	+	0	0	0	0	0	0
2984 F		1	+	0	0	0	0	0	0	0	0
3162 F		0	0	0	0	0	0	0	0	0	0
2986 F		+	1	0	0	0	0	0	0	0	0
2987 F		+	+	0	0	0	0	0	0	0	0
2988 F		+	+	0	0	0	0	0	0	0	0

^aScored using the scale presented in Appendix B.

M=Male

F=Female

TABLE IIC (cont.)

A CLOSED-PATCH REPEATED INSULT DERMAL SENSITIZATION STUDY IN
GUINEA PIGS

INDIVIDUAL DERMAL SCORES AT CHALLENGE^a

GROUP: IVB

INDUCTION MATERIAL: IPDI
CONCENTRATION: 90 mM

Animal No. and Sex	Interval (Hr):	Challenge Concentration (mM):									
		90		30		9.0		0.9		0.09	
		24	48	24	48	24	48	24	48	24	48
2720 M		+	+	0	0	0	0	0	0	0	0
2721 M		1	+	0	0	0	0	0	0	0	0
2722 M		1	+	+	0	0	0	0	0	0	0
2885 M		+	+	0	0	0	0	0	0	0	0
2724 M		+	0	0	0	0	0	0	0	0	0
2725 M		0	0	0	0	0	0	0	0	0	0
2726 M		1	1	+	+	0	0	0	0	0	0
2727 M		+	1	+	+	0	0	0	0	0	0
2966 F		+	+	0	0	0	0	0	0	0	0
2967 F		+	+	0	0	0	0	0	0	0	0
2968 F		0	0	0	0	0	0	0	0	0	0
3163 F		0	0	0	0	0	0	0	0	0	0
2970 F		+	+	0	+	0	0	0	0	0	0
2971 F		+	+	0	0	0	0	0	0	0	0
2972 F		+	+	0	0	0	0	0	0	0	0

^aScored using the scale presented in Appendix B.

M=Male

F=Female

TABLE IIC (cont.)

A CLOSED-PATCH REPEATED INSULT DERMAL SENSITIZATION STUDY IN
GUINEA PIGS

INDIVIDUAL DERMAL SCORES AT CHALLENGE^a

GROUP: IVC

INDUCTION MATERIAL: IPDI
CONCENTRATION: 300 mM

Animal No. and Sex	Interval (hr):	Challenge Concentration (mM):									
		90		30		9.0		0.9		0.09	
		24	48	24	48	24	48	24	48	24	48
2728 M		+	0	0	0	0	0	0	0	0	0
2729 M		1	+	+	0	0	0	0	0	0	0
2730 M		1	+	0	0	0	0	0	0	0	0
2731 M		0	0	0	0	0	0	0	0	0	0
2732 M		+	+	0	0	0	0	0	0	0	0
2733 M		2	1	+	0	0	0	0	0	0	0
2734 M		1	+	0	0	0	0	0	0	0	0
2973 F		+	0	0	0	0	0	0	0	0	0
2974 F		1	+	+	+	0	0	0	0	0	0
2975 F		+	0	0	0	0	0	0	0	0	0
2976 F	2,Ed	1	0	0	0	0	0	0	0	0	0
2977 F		1	+	0	+	0	0	0	0	0	0
2978 F		2	1	1	+	0	0	0	0	0	0
2980 F		1	+	0	0	0	0	0	0	0	0
2981 F		1	1	0	0	0	0	0	0	0	0

^aScored using the scale presented in Appendix B.

M=Male
F=Female
Ed=Edema

TABLE IIC (cont.)

A CLOSED-PATCH REPEATED INSULT DERMAL SENSITIZATION STUDY IN
GUINEA PIGS

INDIVIDUAL DERMAL SCORES AT CHALLENGE^a

GROUP: IVD

INDUCTION MATERIAL: None (Irritation Control)

CHALLENGE MATERIAL: IPDI

Animal No. and Sex	Interval (Hr):	Challenge Concentration (mM):									
		90		30		9.0		0.9		0.09	
		24	48	24	48	24	48	24	48	24	48
2901 M		0	0	0	0	0	0	0	0	0	0
2902 M		0	0	0	0	0	0	0	0	0	0
2903 M		0	0	0	0	0	0	0	0	0	0
3152 F		0	0	0	0	0	0	0	0	0	0
3153 F		0	0	0	0	0	0	0	0	0	0
3154 F		0	0	0	0	0	0	0	0	0	0

^aScored using the scale presented in Appendix B.

M=Male

F=Female

TABLE IIC (cont.)

A CLOSED-PATCH REPEATED INSULT DERMAL SENSITIZATION STUDY IN
GUINEA PIGS

INDIVIDUAL DERMAL SCORES AT CHALLENGE^a

GROUP: VA

INDUCTION MATERIAL: m-TMXDI
CONCENTRATION: 10 mM

Animal No. and Sex	Interval (Hr):	Challenge Concentration (mM):									
		30		10		3.0		0.3		0.03	
		24	48	24	48	24	48	24	48	24	48
2830 M		1	1	+	+	0	0	0	0	0	0
2831 M		+	+	0	0	0	0	0	0	0	0
2832 M		0	+	+	+	0	0	0	0	0	0
2833 M		0	0	0	0	0	0	0	0	0	0
2834 M		+	+	0	0	0	0	0	0	0	0
2835 M		+	1	0	0	0	0	0	0	0	0
2836 M		+	+	0	0	0	0	0	0	0	0
2837 M		+	+	0	0	0	0	0	0	0	0
3077 F		+	+	+	0	0	0	0	0	0	0
3078 F		0	0	0	0	0	0	0	0	0	0
3079 F		+	+	0	0	0	0	0	0	+	+
3080 F		+	1	0	0	0	0	0	0	0	0
3081 F		0	0	0	0	0	0	0	0	0	0
3137 F		+	+	0	0	0	0	0	0	0	0
3083 F		0	0	0	0	0	0	0	0	0	0

^aScored using the scale presented in Appendix B.

M=Male

F=Female

TABLE IIC (cont.)

A CLOSED-PATCH REPEATED INSULT DERMAL SENSITIZATION STUDY IN
GUINEA PIGS

INDIVIDUAL DERMAL SCORES AT CHALLENGE^a

GROUP: VB

INDUCTION MATERIAL: m-TMXDI
CONCENTRATION: 30 mM

Animal No. and Sex	Interval (Hr):	Challenge Concentration (mM):									
		30		10		3.0		0.3		0.03	
		24	48	24	48	24	48	24	48	24	48
2823 M		+	+	+	0	0	0	0	0	0	0
2824 M		0	0	0	0	0	0	0	0	0	0
2825 M		1	1	+	0	0	0	0	0	0	0
2826 M		1	1	0	+	0	0	0	0	0	0
2827 M		2	1	1	+	+	+	0	0	0	0
2828 M		1	+	+	+	0	0	0	0	0	0
2829 M		+	+	0	0	0	0	0	0	0	0
3069 F		1	1	1	1	0	0	0	0	0	0
3136 F		0	0	0	0	0	0	0	0	0	0
3071 F		+	+	0	0	0	0	0	0	0	0
3072 F		1	1	+	+	0	0	0	0	0	0
3073 F		0	0	0	0	0	0	0	0	0	0
3074 F		0	0	0	0	0	0	0	0	0	0
3075 F		+	+	0	0	0	0	0	0	0	0
3076 F		+	+	0	0	0	0	0	0	0	0

^aScored using the scale presented in Appendix B.

M=Male

F=Female

TABLE IIC (cont.)

A CLOSED-PATCH REPEATED INSULT DERMAL SENSITIZATION STUDY IN
GUINEA PIGS

INDIVIDUAL DERMAL SCORES AT CHALLENGE^a

GROUP: VC

INDUCTION MATERIAL: m-TMXDI
CONCENTRATION: 100 mM

Animal No. and Sex	Interval (Hr):	Challenge Concentration (mM):									
		30		10		3.0		0.3		0.03	
		24	48	24	48	24	48	24	48	24	48
2814 M		2	1	1	1	0	0	0	0	0	0
2815 M		+	+	0	0	0	0	0	0	0	0
2816 M		+	+	0	0	0	0	0	0	0	0
2817 M		2	2	2	1	1	1	0	0	0	0
2818 M		1	+	+	0	0	0	0	0	0	0
2819 M		1	+	+	+	0	0	0	0	0	0
2821 M		2	1	1	+	+	0	0	0	0	0
2822 M		+	+	+	0	0	0	0	0	0	0
3062 F		1	1	+	+	0	0	0	0	0	0
3063 F		1	+	0	0	0	0	0	0	0	0
3064 F		1	1	+	+	0	0	0	0	0	0
3065 F		1	+	0	0	0	0	0	0	0	0
3066 F		+	+	0	0	0	0	0	0	0	0
3067 F		1	1	0	+	0	0	0	0	0	0
3068 F		+	0	0	0	0	0	0	0	0	0

^aScored using the scale presented in Appendix B.

M=Male

F=Female

TABLE IIC (cont.)

A CLOSED-PATCH REPEATED INSULT DERMAL SENSITIZATION STUDY IN
GUINEA PIGS

INDIVIDUAL DERMAL SCORES AT CHALLENGE^a

GROUP: VD

INDUCTION MATERIAL: None (Irritation Control)
CHALLENGE MATERIAL: m-TMXDI

Animal No. and Sex	Interval (Hr):	Challenge Concentration (mM):									
		30		10		3.0		0.3		0.03	
		24	48	24	48	24	48	24	48	24	48
2904 M		0	0	0	0	0	0	0	0	0	0
2905 M		0	0	0	0	0	0	0	0	0	0
2906 M		0	0	0	0	0	0	0	0	0	0
3155 F		0	0	0	0	0	0	0	0	0	0
3156 F		0	0	0	0	0	0	0	0	0	0
3157 F		0	0	0	0	0	0	0	0	0	0

^aScored using the scale presented in Appendix B.

M=Male

F=Female

TABLE IIC (cont.)

A CLOSED-PATCH REPEATED INSULT DERMAL SENSITIZATION STUDY IN
GUINEA PIGS

INDIVIDUAL DERMAL SCORES AT CHALLENGE^a

GROUP: VIA

INDUCTION MATERIAL: HMDI
CONCENTRATION: 20 mM

Animal No. and Sex	Interval (Hr):	Challenge Concentration (mM):									
		60		20		6.0		0.6		0.06	
		24	48	24	48	24	48	24	48	24	48
2838 M		+	+	0	0	0	0	0	0	0	0
2839 M		0	0	0	0	0	0	0	0	0	0
2886 M		1	1	+	+	0	0	0	0	0	0
2841 M		+	+	0	0	0	0	0	0	0	0
2842 M		+	1	0	0	0	0	0	0	0	0
2887 M		0	0	0	0	0	0	0	0	0	0
284 M		0	0	0	0	0	0	0	0	0	0
308 M		0	0	0	0	0	0	0	0	0	0
3085 F		+	+	0	0	0	0	0	0	0	0
3086 F		+	+	0	0	0	0	0	0	0	0
3087 F		0	0	0	0	0	0	0	0	0	0
3131 F		+	+	0	0	0	0	0	0	0	0
3132 F		+	+	0	0	0	0	0	0	0	0
3138 F		0	0	0	0	0	0	0	0	0	0
3091 F		+	+	0	0	0	0	0	0	0	0

^aScored using the scale presented in Appendix B.
M=Male
F=Female

TABLE IIC (cont.)

A CLOSED-PATCH REPEATED INSULT DERMAL SENSITIZATION STUDY IN
GUINEA PIGS

INDIVIDUAL DERMAL SCORES AT CHALLENGE^a

GROUP: VIB

INDUCTION MATERIAL: HMDI
CONCENTRATION: 60 mM

Animal No. and Sex	Interval (Hr):	Challenge Concentration (mM):									
		60		20		6.0		0.6		0.06	
		24	48	24	48	24	48	24	48	24	48
2845 M		1	+	0	0	0	0	0	0	0	0
2846 M		1	+	+	+	0	0	0	0	0	0
2847 M		0	0	0	0	0	0	0	0	0	0
2848 M		0	0	0	0	0	0	0	0	0	0
2849 M		1	+	+	0	0	0	0	0	0	0
2850 M		0	+	0	0	0	0	0	0	0	0
2852 M		+	+	0	0	0	0	0	0	0	0
2888 M		+	+	0	0	0	0	0	0	0	0
3092 F		+	+	0	0	0	0	0	0	0	0
3093 F		1	+	+	+	0	0	0	0	0	0
3094 F	1,Ed	1	0	0	0	0	0	0	0	0	0
3095 F		1	1	+	0	0	0	0	0	0	0
3096 F		+	+	0	0	0	0	0	0	0	0
3097 F		+	+	0	0	0	0	0	0	0	0
3098 F		+	+	+	0	0	0	0	0	0	0

^aScored using the scale presented in Appendix B.

M=Male

F=Female

Ed=Edema

TABLE IIC (cont.)

A CLOSED-PATCH REPEATED INSULT DERMAL SENSITIZATION STUDY IN
GUINEA PIGS

INDIVIDUAL DERMAL SCORES AT CHALLENGE^a

GROUP: VIC

INDUCTION MATERIAL: HMDI
CONCENTRATION: 200 mM

Animal No. and Sex	Interval (Hr):	Challenge Concentration (mM):									
		60		20		6.0		0.6		0.06	
		24	48	24	48	24	48	24	48	24	48
2854 M		1	1	0	0	0	0	0	0	0	0
2855 M		1	1	+	+	0	0	0	0	0	0
2856 M		2,Ed	1	1	+	0	0	0	0	0	0
2857 M		+	+	0	0	0	0	0	0	0	0
2858 M		0	+	0	0	0	0	0	0	0	0
2859 M		1	+	0	0	0	0	0	0	0	0
2860 M		1	+	0	0	0	0	0	0	0	0
3099 F		1	+	0	0	0	0	0	0	0	0
3100 F		2,Ed	1	0	0	0	0	0	0	0	0
3101 F		1	+	0	0	0	0	0	0	0	0
3102 F		1	1	0	0	0	0	0	0	0	0
3103 F		2,Ed	1	+	+	0	0	0	0	0	0
3104 F		1	+	+	+	0	0	0	0	0	0
3105 F		2,Ed	1	+	+	0	0	0	0	0	0
3106 F		+	1	0	0	0	0	0	0	0	0

^aScored using the scale presented in Appendix B.

M=Male

F=Female

Ed=Edema

TABLE IIC (cont.)

A CLOSED-PATCH REPEATED INSULT DERMAL SENSITIZATION STUDY IN
GUINEA PIGS

INDIVIDUAL DERMAL SCORES AT CHALLENGE^a

GROUP: VID

INDUCTION MATERIAL: None (Irritation Control)

CHALLENGE MATERIAL: HMDI

Animal No. and Sex	Interval (Hr):	Challenge Concentration (mM):									
		60		20		6.0		0.6		0.06	
		24	48	24	48	24	48	24	48	24	48
2907 M		0	0	0	0	0	0	0	0	0	0
2908 M		0	+	0	0	0	0	0	0	0	0
2909 M		0	+	0	0	0	0	0	0	0	0
3158 F		0	0	0	0	0	0	0	0	0	0
3159 F		0	0	0	0	0	0	0	0	0	0
3160 F		0	0	0	0	0	0	0	0	0	0

^aScored using the scale presented in Appendix B.

M=Male

F=Female

TABLE IIC (cont.)

A CLOSED-PATCH REPEATED INSULT DERMAL SENSITIZATION STUDY IN
GUINEA PIGS

INDIVIDUAL DERMAL SCORES AT CHALLENGE^a

GROUP: VIIA

INDUCTION MATERIAL: m-TMI
CONCENTRATION: 50 mM

Animal No. and Sex	Interval (Hr):	Challenge Concentration (mM):									
		150		50		15		1.5		0.15	
		24	48	24	48	24	48	24	48	24	48
2876 M		1,Ed	1	0	0	0	0	0	0	0	0
2878 M		1	1	+	+	0	0	0	0	0	0
2879 M		1	1	+	+	0	0	0	0	0	0
2880 M		1	1	+	+	0	0	0	0	0	0
2881 M		0	0	0	0	0	0	0	0	0	0
2882 M		0	0	0	0	0	0	0	0	0	0
2883 M		1	1,Ed	0	+	0	+	0	0	0	0
2884 M		0	+	0	0	0	0	0	0	0	0
3124 F		+	+	0	0	0	0	0	0	0	0
3125 F		+	0	0	0	0	0	0	0	0	0
3126 F		0	+	0	0	0	0	0	0	0	0
3127 F		1	1	+	1	0	0	0	0	0	0
3128 F		0	0	0	0	0	0	0	0	0	0
3129 F		+	+	0	0	0	0	0	0	0	0
3130 F		0	0	0	0	0	0	0	0	0	0

^aScored using the scale presented in Appendix B.

M=Male

F=Female

Ed=Edema

TABLE IIC (cont.)

A CLOSED-PATCH REPEATED INSULT DERMAL SENSITIZATION STUDY IN
GUINEA PIGS

INDIVIDUAL DERMAL SCORES AT CHALLENGE^a

GROUP: VIIB

INDUCTION MATERIAL: m-TMI
CONCENTRATION: 150 mM

Animal No. and Sex	Interval (Hr):	Challenge Concentration (mM):									
		150		50		15		1.5		0.15	
		24	48	24	48	24	48	24	48	24	48
2869 M		1	+	+	0	0	0	0	0	0	0
2870 M		+	+	0	+	0	0	0	0	0	0
2871 M		+	+	0	0	0	0	0	0	0	0
2872 M		1,Ed	1	+	0	0	0	0	0	0	0
2873 M		+	+	0	0	0	0	0	0	0	0
2874 M		1	1	0	0	0	0	0	0	0	0
2875 M		1	+	0	0	0	0	0	0	0	0
3115 F		+	+	0	0	0	0	0	0	0	0
3116 F		+	+	0	0	0	0	0	0	0	0
3117 F		1	+	+	0	0	0	0	0	0	0
3118 F		0	+	0	0	0	0	0	0	0	0
3119 F		+	+	0	0	0	0	0	0	0	0
3120 F		+	+	0	0	0	0	0	0	0	0
3121 F		1	1	0	0	0	0	0	0	0	0
3122 F		+	+	0	0	0	0	0	0	0	0

^aScored using the scale presented in Appen x B.

M=Male

F=Female

Ed=Edema

TABLE IIC (cont.)

A CLOSED-PATCH REPEATED INSULT DERMAL SENSITIZATION STUDY IN
GUINEA PIGS

INDIVIDUAL DERMAL SCORES AT CHALLENGE^a

GROUP: VIIC

INDUCTION MATERIAL: m-TMI
CONCENTRATION: 500 mM

Animal No. and Sex	Interval (Hr):	Challenge Concentration (mM):									
		150		50		15		1.5		0.15	
		24	48	24	48	24	48	24	48	24	48
2861 M		2	1	1	+	0	0	0	0	0	0
2862 M		1,Ed	+	0	0	0	0	0	0	0	0
2863 M		2	1	+	+	0	0	0	0	0	0
2864 M		3,Ed	2	2	1	+	+	0	0	0	0
2865 M		1	1	+	+	0	0	0	0	0	0
2866 M		1	1	0	+	0	0	0	0	0	0
2867 M		1	+	0	0	0	0	0	0	0	0
2868 M		2,Ed	1	+	+	0	0	0	0	0	0
3107 F		2,Ed	1,Ed	1	1	+	0	0	0	0	0
3108 F		2,Ed	2	1	+	0	0	0	0	0	0
3110 F		3,Ed	2	3,Ed	2,Ed	2	1	0	0	0	0
3111 F		1	1	+	+	0	0	0	0	0	0
3112 F		1,Ed	1	0	0	0	0	0	0	0	0
3113 F		2,Ed	2,Ed	1,Ed	1,Ed	+	0	0	0	0	0
3114 F		2	1	+	+	0	0	0	0	0	0

^aScored using the scale presented in Appendix B.

M=Male
F=Female
Ed=Edema

TABLE IIC (cont.)

A CLOSED-PATCH REPEATED INSULT DERMAL SENSITIZATION STUDY IN
GUINEA PIGS

INDIVIDUAL DERMAL SCORES AT CHALLENGE^a

GROUP: VIID

INDUCTION MATERIAL: None (Irritation Control)
CHALLENGE MATERIAL: m-TMI

Animal No. and Sex	Interval (Hr):	Challenge Concentration (mM):									
		150		50		15		1.5		0.15	
		24	48	24	48	24	48	24	48	24	48
2910 M		0	0	0	0	0	0	0	0	0	0
2911 M		0	0	0	0	0	0	0	0	0	0
2912 M		0	0	0	0	0	0	0	0	0	0
3161 F		0	0	0	0	0	0	0	0	0	0
3165 F		0	0	0	0	0	0	0	0	0	0
3166 F		0	0	0	0	0	0	0	0	0	0

^aScored using the scale presented in Appendix B.
M=Male
F=Female

TABLE IIIA
A CLOSED-PATCH REPEATED INSULT DERMAL SENSITIZATION STUDY IN
GUINEA PIGS

SUMMARY OF RESPONSES TO CROSS-CHALLENGE^a

Group	Induction Material	Cross-Challenge Material	Conc. (mM)	Hr:	Derma1 Score					Edema
					0	+	1	2	3	
IC	TDI	p-TMXDI	60	24	13	2	-	-	-	-
				48	14	1	-	-	-	-
		m-TMXDI	30	24	15	-	-	-	-	-
				48	15	-	-	-	-	-
		m-TMI	150	24	13	2	-	-	-	-
				48	15	-	-	-	-	-
		MDI	30	24	15	-	-	-	-	-
				48	15	-	-	-	-	-
				24	15	-	-	-	-	-
				48	15	-	-	-	-	-
IIC	MDI	p-TMXDI ^b	60	24	12	2	-	-	-	-
				48	13	1	-	-	-	-
		m-TMXDI	30	24	15	-	-	-	-	-
				48	15	-	-	-	-	-
		m-TMI ^b	150	24	14	-	-	-	-	-
				48	14	-	-	-	-	-
		TDI	90	24	15	-	-	-	-	-
				48	15	-	-	-	-	-
				24	15	-	-	-	-	-
				48	15	-	-	-	-	-
IIIC	p-TMXDI	IPDI	90	24	11	4	-	-	-	-
				48	11	3	1	-	-	-
		m-TMXDI	30	24	12	3	-	-	-	-
				48	14	1	-	-	-	-
		HMDI	60	24	15	-	-	-	-	-
				48	14	1	-	-	-	-
		m-TMI	150	24	12	1	2	-	-	-
				48	13	1	1	-	-	-
				24	12	1	2	-	-	-
				48	13	1	1	-	-	-
IVC	IPDI	p-TMXDI	60	24	10	4	1	-	-	-
				48	8	6	1	-	-	-
		m-TMXDI	30	24	15	-	-	-	-	-
				48	13	2	-	-	-	-
		HMDI	60	24	15	-	-	-	-	-
				48	13	2	-	-	-	-
		m-TMI	150	24	15	-	-	-	-	-
				48	15	-	-	-	-	-
				24	15	-	-	-	-	-
				48	15	-	-	-	-	-

^aNumbers presented are numbers of animals with indicated score. See Appendix B for scoring system. N=15 per group unless indicated otherwise.

^bOne animal not scored because patch removed during exposure period.

TABLE IIIA (cont.)

A CLOSED-PATCH REPEATED INSULT DERMAL SENSITIZATION STUDY IN
GUINEA PIGS

SUMMARY OF RESPONSES TO CROSS-CHALLENGE^a

Group	Induction Material	Cross- Challenge Material	Conc. (mM)	Hr:	Dermal Score					Edema
					0	+	1	2	3	
VC	m-TMXDI	p-TMXDI	60	24	6	6	3	-	-	-
				48	3	11	1	-	-	-
		IPDI	90	24	13	2	-	-	-	-
				48	9	6	-	-	-	-
		HMDI	60	24	14	1	-	-	-	-
				48	11	4	-	-	-	-
VIC	HMDI	p-TMXDI	60	24	12	3	-	-	-	-
				48	13	2	-	-	-	-
		IPDI	90	24	12	3	-	-	-	-
				48	8	6	1	-	-	-
		m-TMXDI	30	24	15	-	-	-	-	-
				48	14	1	-	-	-	-
VIIC	m-TMI	m-TMI	150	24	14	-	1	-	-	-
				48	14	-	1	-	-	-
		p-TMXDI	60	24	2	6	5	2	-	1
				48	3	7	4	1	-	-
		IPDI	90	24	12	3	-	-	-	-
				48	9	6	-	-	-	-
VIIC	m-TMI	m-TMXDI	30	24	12	2	1	-	-	-
				48	11	4	-	-	-	-
		HMDI	60	24	15	-	-	-	-	-
				48	14	-	1	-	-	-
				24	15	-	-	-	-	-
				48	14	-	1	-	-	-

^aNumbers presented are numbers of animals with indicated score. See Appendix B for scoring system. N=15 per group unless indicated otherwise.

TABLE IIIA (cont.)

A CLOSED-PATCH REPEATED INSULT DERMAL SENSITIZATION STUDY IN
GUINEA PIGS

SUMMARY OF RESPONSES TO CROSS-CHALLENGE^a

Group	Induction Material	Cross- Challenge Material	Conc. (mM)	Hr:	Dermal Score					Edema
					0	+	1	2	3	
E ^C	None (Irritation Control)	TDI	90	24	5	1	-	-	-	-
				48	5	1	-	-	-	-
		MDI	30	24	6	-	-	-	-	-
				48	6	-	-	-	-	-
		p-TMXDI	60	24	6	-	-	-	-	-
				48	6	-	-	-	-	-
		IPDI	90	24	6	-	-	-	-	-
				48	6	-	-	-	-	-
		m-TMXDI	30	24	6	-	-	-	-	-
				48	6	-	-	-	-	-
		f-MDI	60	24	6	-	-	-	-	-
				48	6	-	-	-	-	-
		m-TMI	150	24	6	-	-	-	-	-
				48	6	-	-	-	-	-

^aNumbers presented are numbers of animals with indicated score. See
Appendix B for scoring system. N=15 per group unless indicated otherwise.
CN=6

TABLE IIIB

A CLOSED-PATCH REPEATED INSULT DERMAL SENSITIZATION STUDY IN
GUINEA PIGS

INDIVIDUAL DERMAL SCORES AT CROSS-CHALLENGE^a

GROUP: IC

INDUCTION MATERIAL: TDI
CONCENTRATION: 300 mM

Animal No. and Sex	Test Material: Conc. (mM): Interval (Hr):	p-TMXDI		m-TMXDI		m-TMI		MDI	
		60		30		150		30	
		24	48	24	48	24	48	24	48
2807 M		0	0	0	0	0	0	0	0
2808 M		0	0	0	0	0	0	0	0
2809 M		0	0	0	0	+	0	0	0
2810 M		0	0	0	0	0	0	0	0
2811 M		+	+	0	0	0	0	0	0
2812 M		0	0	0	0	0	0	0	0
2813 M		0	0	0	0	0	0	0	0
3054 F		0	0	0	0	0	0	0	0
3055 F		0	0	0	0	0	0	0	0
3056 F		0	0	0	0	0	0	0	0
3134 F		+	0	0	0	0	0	0	0
3058 F		0	0	0	0	0	0	0	0
3059 F		0	0	0	0	+	0	0	0
3060 F		0	0	0	0	0	0	0	0
3061 F		0	0	0	0	0	0	0	0

^aScored using the scale presented in Appendix B.

M=Male

F=Female

TABLE IIIB (cont.)

A CLOSED-PATCH REPEATED INSULT DERMAL SENSITIZATION STUDY IN
GUINEA PIGS

INDIVIDUAL DERMAL SCORES AT CROSS-CHALLENGE^a

GROUP: IIC

INDUCTION MATERIAL: MDI
CONCENTRATION: 100 mM

Animal No. and Sex	Test Material: Conc. (mM): Interval (Hr):	p-TMXDI		m-TMXDI		m-TMI		TDI	
		60		30		150		90	
		24	48	24	48	24	48	24	48
2775 M		0	0	0	0	0	0	0	0
2776 M		0	0	0	0	0	0	0	0
2777 M		0	0	0	0	0	0	0	0
2778 M		0	0	0	0	0	0	0	0
2779 M		0	0	0	0	0	0	0	0
2780 M		0	0	0	0	0	0	0	0
2781 M		0	0	0	0	0	0	0	0
3022 F		+	+	0	0	0	0	0	0
3023 F		0	0	0	0	0	0	0	0
3135 F		0	0	0	0	0	0	0	0
3025 F		0	0	0	0	0	0	0	0
3026 F		b	b	0	0	b	b	0	0
3027 F		+	0	0	0	0	0	0	0
3028 F		0	0	0	0	0	0	0	0
3029 F		0	0	0	0	0	0	0	0

^aScored using the scale presented in Appendix B.

^bNot evaluated, patches missing, dose site not discernable.

M=Male

F=Female

TABLE IIIB (cont.)

A CLOSED-PATCH REPEATED INSULT DERMAL SENSITIZATION STUDY IN
GUINEA PIGS

INDIVIDUAL DERMAL SCORES AT CROSS-CHALLENGE^a

GROUP: IIIC

INDUCTION MATERIAL: p-TMXDI
CONCENTRATION: 200 mM

Animal No. and Sex	Test Material: Conc. (mM): Interval (Hr):	IPDI		m-TMXDI		HMDI		m-TMI	
		90		30		60		150	
		24	48	24	48	24	48	24	48
2792 M		0	0	0	0	0	0	1	1
2793 M		+	+	0	0	0	0	0	0
2794 M		+	1	0	0	0	0	0	0
2795 M		0	0	0	0	0	0	0	0
2796 M		0	0	0	0	0	0	0	0
2797 M		0	0	+	0	0	0	0	0
2798 M		0	0	0	0	0	0	0	0
3038 F		0	0	0	+	0	0	0	0
3039 F		+	+	0	0	0	+	0	0
3040 F		0	0	0	0	0	0	1	+
3041 F		0	0	+	0	0	0	0	0
3042 F		0	0	+	0	0	0	+	0
3044 F		0	0	0	0	0	0	0	0
3045 F		0	0	0	0	0	0	0	0
3046 F		+	+	0	0	0	0	0	0

^aScored using the scale presented in Appendix B.

M=Male

F=Female

TABLE III B (cont.)

A CLOSED-PATCH REPEATED INSULT DERMAL SENSITIZATION STUDY IN
GUINEA PIGS

INDIVIDUAL DERMAL SCORES AT CROSS-CHALLENGE^a

GROUP: IVC

INDUCTION MATERIAL: IPDI

CONCENTRATION: 300 mM

Animal No. and Sex	Test Material: Conc. (mM): Interval (Hr):	p-TMXDI		m-TMXDI		HMDI		m-TMI	
		60		30		60		150	
		24	48	24	48	24	48	24	48
2728 M		0	0	0	0	0	0	0	0
2729 M		+	+	0	+	0	0	0	0
2730 M		0	0	0	0	0	0	0	0
2731 M		1	+	0	0	0	0	0	0
2732 M		0	0	0	0	0	0	0	0
2733 M		0	0	0	0	0	0	0	0
2734 M		0	0	0	0	0	0	0	0
2973 F		0	+	0	0	0	0	0	0
2974 F		+	+	0	+	0	0	0	0
2975 F		0	0	0	0	0	0	0	0
2976 F		0	0	0	0	0	+	0	0
2977 F		0	+	0	0	0	0	0	0
2978 F		+	1	0	0	0	+	0	0
2980 F		0	0	0	0	0	0	0	0
2981 F		+	+	0	0	0	0	0	0

^aScored using the scale presented in Appendix B.

M=Male

F=Female

TABLE IIIB (cont.)

A CLOSED-PATCH REPEATED INSULT DERMAL SENSITIZATION STUDY IN
GUINEA PIGS

INDIVIDUAL DERMAL SCORES AT CROSS-CHALLENGE^a

GROUP: VC

INDUCTION MATERIAL: m-TMXDI
CONCENTRATION: 100 mM

Animal No. and Sex	Test Material: Conc. (mM): Interval (Hr):	p-TMXDI		IPDI		HMDI		m-TMI	
		60		90		60		150	
		24	48	24	48	24	48	24	48
2814 M		1	+	0	+	0	+	+	+
2815 M		0	+	0	0	0	0	+	+
2816 M		+	+	0	0	0	0	0	0
2817 M		+	+	0	0	0	0	+	+
2818 M		1	1	0	+	+	+	2	1
2819 M		0	+	0	0	0	0	0	0
2821 M		0	+	0	+	0	0	+	+
2822 M		+	0	0	0	0	0	0	0
3062 F		+	+	+	+	0	+	+	+
3063 F		+	+	0	0	0	0	+	0
3064 F		0	+	0	+	0	+	+	+
3065 F		+	+	0	0	0	0	0	0
3066 F		0	0	0	0	0	0	0	0
3067 F		1	+	+	+	0	0	+	+
3068 F		0	0	0	0	0	0	0	0

^aScored using the scale presented in Appendix B.
M=Male
F=Female

TABLE IIIB (cont.)

A CLOSED-PATCH REPEATED INSULT DERMAL SENSITIZATION STUDY IN
GUINEA PIGS

INDIVIDUAL DERMAL SCORES AT CROSS-CHALLENGE^a

GROUP: VIC

INDUCTION MATERIAL: HMDI
CONCENTRATION: 200 mM

Animal No. and Sex	Test Material: Conc. (mM): Interval (Hr):	p-TMXDI		IPDI		m-TMXDI		m-TMI	
		60		90		30		150	
		24	48	24	48	24	48	24	48
2854 M		0	0	0	0	0	0	0	0
2855 M		0	0	0	+	0	0	0	0
2856 M		0	0	0	0	0	0	0	0
2857 M		0	0	0	0	0	0	0	0
2858 M		0	0	0	0	0	0	0	0
2859 M		0	0	0	0	0	0	0	0
2860 M		0	0	0	0	0	0	0	0
3099 F		0	0	0	+	0	0	0	0
3100 F		0	0	+	+	0	0	0	0
3101 F		0	0	0	+	0	0	0	0
3102 F		+	+	+	+	0	0	0	0
3103 F		+	0	0	0	0	0	0	0
3104 F		+	+	+	1	0	+	1	1
3105 F		0	0	0	+	0	0	0	0
3106 F		0	0	0	0	0	0	0	0

^aScored using the scale presented in Appendix B.

M=Male

F=Female

TABLE IIIB (cont.)

A CLOSED-PATCH REPEATED INSULT DERMAL SENSITIZATION STUDY IN
GUINEA PIGS

INDIVIDUAL DERMAL SCORES AT CROSS-CHALLENGE^a

GROUP: VIIC INDUCTION MATERIAL: m-TMI
CONCENTRATION: 500 mM

Animal No and Sex	Test Material: Conc. (mM): Interval (Hr):	p-TMXDI 60		IPDI 90		m-TMI DI 30		HMDI 60	
		24	48	24	48	24	48	24	48
2861 M		2,Ed	2	+	+	1	+	0	0
2862 M		+	+	0	0	0	0	0	0
2863 M		1	1	+	+	+	+	0	0
2864 M		2	1	+	+	0	0	0	0
2865 M		+	+	0	0	0	0	0	0
2866 M		0	0	0	0	0	0	0	0
2867 M		+	0	0	0	0	0	0	0
2868 M		1	+	0	0	0	0	0	0
3107 F		1	1	0	+	0	0	0	0
3108 F		+	+	0	0	0	0	0	0
3110 F		1	+	0	0	0	+	0	0
3111 F		+	+	0	0	0	0	0	0
3112 F		0	0	0	+	0	0	0	0
3113 F		1	1	0	0	0	0	0	0
3114 F		+	+	0	+	+	+	0	1

^aScored using the scale presented in Appendix B.

M=Male
F=Female
Ed=Edema

TABLE IIIB (cont.)

A CLOSED-PATCH REPEATED INSULT DERMAL SENSITIZATION STUDY IN
GUINEA PIGS

INDIVIDUAL DERMAL SCORES AT CROSS-CHALLENGE^a

GROUP: E		INDUCTION MATL		None (Irritation Control)					
Animal No. and Sex	Test Material: Conc. (mM): Interval (Hr):	TDI		MDI		p-TMXDI		IPDI	
		90		30		60		90	
		24	48	24	48	24	48	24	48
2913 M		0	0	0	0	0	0	0	0
2914 M		0	0	0	0	0	0	0	0
2915 M		0	0	0	0	0	0	0	0
3167 F		+	+	0	0	0	0	0	0
3168 F		0	0	0	0	0	0	0	0
2979 F		0	0	0	0	0	0	0	0

^aScored using the scale presented in Appendix B.

M=Male

F=Female

TABLE IIIIB (cont.)

A CLOSED-PATCH REPEATED INSULT DERMAL SENSITIZATION STUDY IN
GUINEA PIGS

INDIVIDUAL DERMAL SCORES AT CROSS-CHALLENGE^a

GROUP: E (cont.) INDUCTION MATERIAL: None (Irritation Control)

Animal No. and Sex	Test Material: Conc. (mM): Interval (Hr):	m-TMXDI		HMDI		m-TMI	
		30		60		150	
		24	48	24	48	24	48
2916 M		0	0	0	0	0	0
2917 M		0	0	0	0	0	0
2918 M		0	0	0	0	0	0
2996 F		0	0	0	0	0	0
3005 F		0	0	0	0	0	0
3043 F		0	0	0	0	0	0

^aScored using the scale presented in Appendix B.
M=Male
F=Female

APPENDIX A
A CLOSED-PATCH REPEATED INSULT DERMAL SENSITIZATION STUDY
IN GUINEA PIGS
RANGE-FINDING DATA - DERMAL SCORES^a
TEST MATERIAL: TDI

I. VEHICLE: OLIVE OIL

Animal No./Sex	Conc.: Day	0.003M			0.01M			0.03M			0.1M			0.3M			1.0M		
		1	2	6	1	2	6	1	2	6	1	2	6	1	2	6	1	2	6
2681	M	0	0	0	0	0	0	0	0	0	0	0	0	1	+	+	2,Ed	1,Ed	2,Ed,D
2682	M	0	0	0	0	0	0	0	0	0	+	+	0	1,Ed	+	1	1,Ed	1,Ed	1,Ed,D
2703	M	0	0	0	0	0	0	0	0	0	+	+	0	1	+	+	2,Ed	1,Ed	2,Ed,D
2928	F	0	0	0	0	0	0	0	0	0	0	0	0	1,Ed	1	+	1,Ed	1,Ed	1,Ed,D
2929	F	0	0	0	0	0	0	0	0	0	+	0	0	1	1	+	2,Ed	1,Ed	1,Ed,D
2930	F	0	0	0	0	0	0	0	0	0	0	0	0	+	+	+	1,Ed	1,Ed	1,Ed,D

II. VEHICLE: OLIVE OIL/ACETONE (1:1)

Animal No./Sex	Conc.: Day	0.03M			0.1M			0.3M		
		1	2	4	1	2	4	1	2	4
2708	M	0	0	0	0	0	0	+	+	+
2709	M	0	0	0	0	0	0	0	0	0
2710	M	0	0	0	0	0	0	0	+	+
2953	F	0	0	0	0	0	0	0	0	0
2954	F	0	0	0	0	0	0	0	0	+,D
2956	F	0	0	0	0	0	0	0	0	0

M = Male, F = Female; Ed = Edema; D = Desquamation.
^aScored using the scale presented in Appendix B.

Revised Page: CSA 1000 Date: 4/9/85

A-1
4971-84

APPENDIX A (CONT.)

A CLOSED-PATCH REPEATED INSULT DERMAL SENSITIZATION STUDY

IN GUINEA PIGS

RANGE-FINDING DATA - DERMAL SCORES^a

TEST MATERIAL: MDI

VEHICLE: OLIVE OIL/ACETONE (1:1)																			
Animal No./Sex	Conc.: Day :	0.003M			0.01M			0.03M			0.1M			0.3M			1.0M		
		1	2	5	1	2	5	1	2	5	1	2	5	1	2	5			
2699	M	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	+	+	+
2700	M	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	+	+	± D
2701	M	0	0	0	0	0	0	0	0	0	0	+	±,D	0	+	±,D	+	1,Ed	2,Ed,D
2950	F	0	0	0	0	0	0	0	0	0	0	0	±	0	0	1	+	±	1,D
2947	F	0	0	0	0	0	0	0	0	0	0	+	±	0	+	1,D	+	±	±,Ed,D
2948	F	0	0	0	0	0	0	0	0	0	0	0	0	0	0	±	0	0	±

M = Male, F = Female; Ed = Edema, D = Desquamation.
^aScored using the scale presented in Appendix B.

APPENDIX A (CONT.)

A CLOSED-PATCH REPEATED INSULT DERMAL SENSITIZATION STUDY

IN GUINEA PIGS

RANGE-FINDING DATA - DERMAL SCORES^a

TEST MATERIAL: P-TMXDI

VEHICLE: OLIVE OIL/ACETONE (1:1)																			
Animal No./Sex	Conc.: Day :	0.003M			0.01M			0.03M			0.1M			0.3M			1.0M		
		1	2	5	1	2	5	1	2	5	1	2	5	1	2	5	1	2	5
2696	M	0	0	0	0	0	0	0	0	0	0	0	0	+	+	+,D	1,Ed	+	1,Ed,D
2697	M	0	0	0	0	0	0	0	0	0	0	0	0	+	0	+,D	+,Ed	+	1,D
2698	M	0	0	0	0	0	0	0	0	0	0	0	0	+	0	+,D	+	+	+,D
2943	F	0	0	0	0	0	0	0	0	0	0	0	0	+	+	+,D	+,Ed	+	+,D
2944	F	0	0	0	0	0	0	0	0	0	0	0	0	+	0	+,D	1,Ed	1,Ed	+,Ed,D
2945	F	0	0	0	0	0	0	0	0	0	0	0	0	+	+	+,D	+,Ed	+,Ed	+,D

M = Male, F = Female; Ed = Edema; D = Desquamation.
^aScored using the scale presented in Appendix B.

APPENDIX A (CONT.)

A CLOSED-PATCH REPEATED INSULT DERMAL SENSITIZATION STUDY

IN GUINEA PIGS

RANGE-FINDING DATA - DERMAL SCORES^a

TEST MATERIAL: IPDI

I. VEHICLE: OLIVE OIL

Animal No./Sex	Conc.: Day :	0.003M			0.01M			0.03M			0.1M			0.3M			1.0M		
		1	2	6	1	2	6	1	2	6	1	2	6	1	2	6	1	2	6
2684	M	0	0	0	+	0	0	0	0	0	0	0	0	1	1	+	2,Ed	2,Ed	1,Ed
2685	M	0	0	0	0	0	0	0	0	0	1	+	0	1,Ed	+	+,D	2,Ed	1,Ed	1,Ed,D
2704	M	0	0	0	0	0	0	0	0	0	+	+	0	1	1	1,D	2,Ed	2,Ed	1,Ed,D
2931	F	0	0	0	0	0	0	0	0	0	+	0	0	+	+	+	2,Ed	1,Ed	1,Ed,D
2932	F	0	0	0	0	0	0	0	0	0	+	+	+	1,Ed	1	1,D	2,Ed	1,Ed	1,Ed,D
2933	F	0	0	0	0	0	0	0	0	0	1	+	+	1	?	1,D	2,Ed	2,Ed	2,Ed,D

II. VEHICLE: OLIVE OIL/ACETONE (1:1)

Animal No./Sex	Conc.: Day :	0.03M			0.1M			0.3M		
		1	2	4	1	2	4	1	2	4
2708	M	+	0	0	0	0	+	+	+	+,D
2709	M	0	0	0	0	0	0	0	0	0,D
2710	M	0	0	0	0	0	+	+	0	+
2953	F	0	0	0	0	0	+	0	0	0
2954	F	0	0	0	0	0	0	0	0	0
2956	F	0	0	0	0	0	0	0	0	0

M = Male, F = Female; Ed = Edema; D = Desquamation.

^aScored using the scale presented in Appendix B.

Revised Page:

CSH/MS

Date:

4/9/85

APPENDIX A (CONT.)

A CLOSED-PATCH REPEATED INSULT DERMAL SENSITIZATION STUDY

IN GUINEA PIGS

RANGE-FINDING DATA - DERMAL SCORES^a

TEST MATERIAL: M-TMXDI

I. VEHICLE: OLIVE OIL

Animal No./Sex	Conc.: Day	0.003M			0.01M			0.03M			0.1M			0.3M			1.0M		
		1	2	6	1	2	6	1	2	6	1	2	6	1	2	6	1	2	6
2687	M	0	0	0	0	0	0	0	0	0	+	+	+	1,Ed	1	+,D	1,Ed	1,Ed	2,Ed,D
2688	M	0	0	0	0	0	0	0	0	0	+	+	+	1,Ed	1	1,D	1,Ed	1,Ed	2,Ed,D
2689	M	0	0	0	0	0	+	0	0	0	0	0	+	1,Ed	+	1,D	2,Ed	1,Ed	2,Ed,D
2934	F	0	0	0	0	0	0	0	0	0	+	+	0	1	+	1,D	1,Ed	1,Ed	2,Ed,D
2935	F	0	0	0	0	0	0	0	0	0	0	0	0	1,Ed	+	+	1,Ed	1,Ed	2,Ed,D
2936	F	0	0	0	0	0	0	0	0	0	0	0	0	+	+	1	1,Ed	+	1,Ed,D

II. VEHICLE: OLIVE OIL/ACETONE (1:1)

Animal No./Sex	Conc.: Day	0.03M			0.1M			0.3M		
		1	2	4	1	2	4	1	2	4
2711	M	0	0	0	+	0	0	+,Ed	+,Ed	1,D
2712	M	0	0	0	+	0	0	+	+	+,D
2713	M	0	0	0	+	+	+	+	0	+
2957	F	0	0	0	0	0	+	0	0	+,D
2958	F	0	0	0	0	0	0	+	+	0,D
2959	F	0	0	0	+	0	+	+	0	+,D

M = Male, F = Female; Ed = Edema; D = Desquamation.

^aScored using the scale presented in Appendix B.

APPENDIX A (CONT.)

A CLOSED-PATCH REPEATED INSULT DERMAL SENSITIZATION STUDY

IN GUINEA PIGS

RANGE-FINDING DATA - DERMAL SCORES^a

TEST MATERIAL: HMDI

I. VEHICLE: OLIVE OIL

Anim. No.	Conc.: Day	0.003M			0.01M			0.03M			0.1M			0.3M			1.0M		
		1	2	6	1	2	6	1	2	6	1	2	6	1	2	6	1	2	6
2690	M	0	0	0	0	0	0	0	0	0	0	0	0	1	1	1,D	1,Ed	1,Ed	1,Ed,D
2691	M	0	0	0	0	0	0	0	0	0	+	+	+,D	1,Ed	1	1,D	2,Ed	1,Ed	2,D
2692	M	0	0	0	0	0	0	0	0	0	0	+	0	1	1	1,D	1,Ed	1,Ed	1,Ed,D
2937	F	0	0	b	0	0	b	0	0	b	0	0	b	+	0	b	1,Ed	1,Ed	b
2938	F	0	0	0	0	0	0	0	+	0	+	1	+	1,Ed	1,Ed	1,Ed,D	2,Ed	2,Ed	2,Ed,D
2939	F	0	0	0	0	0	0	0	+	0	+	1	0	1,Ed	2,Ed	1,Ed,D	2,Ed	1,Ed	1,Ed,D

II. VEHICLE: OLIVE OIL/ACETONE (1:1)

Animal No./Sex	Conc.: Day	0.03M			0.1M			0.3M		
		1	2	4	1	2	4	1	2	4
2711	M	+	0	0,D	0	0	0	+,Ed	+,Ed	1,Ed,D
2712	M	0	0	0	0	0	0	+	+,Ed	+,D
2713	M	0	0	0	0	0	0	+	+	1,D
2957	F	0	0	0	0	0	0	1,Ed	1,Ed	1,Ed,D
2958	F	0	0	0	0	0	0	1,Ed	1,Ed	1,Ed,D
2959	F	0	0	0	0	0	0	+	+	+,D

M = Male, F = Female; Ed = Edema; D = Desquamation.

^aScored using the scale presented in Appendix B.^bAnimal died prior to Day 6.A-6
4971-84

APPENDIX A (CONT.)
A CLOSED-PATCH REPEATED INSULT DERMAL SENSITIZATION STUDY
IN GUINEA PIGS
RANGE-FINDING DATA - DERMAL SCORES^a
TEST MATERIAL: m-TMI

I. VEHICLE: OLIVE OIL

Animal No./Sex	Conc.: Day :	0.003M			0.01M			0.03M			0.1M			0.3M			1.0M		
		1	2	6	1	2	6	1	2	6	1	2	6	1	2	6	1	2	6
2693	M	0	0	0	0	0	0	0	0	0	0	0	0	+	0	+	1,Ed	1	3,Ed,D
2694	M	0	0	0	0	0	0	0	0	0	0	0	0	0	+	+,D	1,Ed	1,Ed	2,Ed,D
2695	M	0	0	0	0	0	0	0	0	0	0	0	0	+	+	+	1,Ed	1,Ed	2,Ed,D
2940	F	0	0	0	0	0	0	0	0	0	+	0	0	0	0	+	1,Ed	1,Ed	2,Ed,D
2941	F	0	0	0	0	0	0	0	0	0	0	0	0	+	+	1	1,Ed	1,Ed	2,Ed,D
2942	F	0	0	0	0	0	0	0	0	0	+	0	0	+	+	+	1,Ed	1,Ed	3,Ed,D

II. VEHICLE: OLIVE OIL/ACETONE (1:1)

Animal No./Sex	Conc.: Day :	0.1M			0.3M			1.0M		
		1	2	4	1	2	4	1	2	4
2714	M	0	0	0	0	0	0	+	+,Ed	+,D
2715	M	0	0	0	0	0	+	1,Ed	1,Ed	2,Ed,D
2716	M	0	0	0	0	0	0	+,Ed	+,Ed	2,Ed,D
2960	F	0	0	0	+	0	+	1,Ed	1,Ed	1,D
2961	F	0	0	0	0	0	0	+,Ed	+,Ed	2,Ed,D
2962	F	0	0	0	0	0	0	1,Ed	1,Ed	1,Ed,D

M = Male, F = Female; Ed = Edema; D = Desquamation.
^aScored using the scale presented in Appendix B.

Revised Page: C. S. Smith Date: 4/9/85

APPENDIX B

DERMAL EVALUATION SCORING SCALE

No reaction.....	0
Very slight (barely perceptible) erythema, usually nonconfluent.....	+
Slight (well-defined) erythema, usually confluent.....	1
Moderate erythema.....	2
Severe erythema, with or without edema, necrosis or eschar formation.....	3

If edema, necrosis, or eschar formation occur, they will also be indicated using the following code:

Edema..... Ed
Necrosis..... N
Eschar..... E
Desquamation. D

Special attention will be given to other dermal change such as leathery skin.

Appendix C

Quality Assurance Statement

Listed below are dates that this study was inspected by the Quality Assurance Unit of Bio/dynamics, Inc. and the dates findings were reported to the Study Director and Management.

<u>Date(s) of Inspection</u>	<u>Reported to Study Director</u>	<u>Reported to Management</u>
4/27/84	4/30/84	5/4/84, 5/7/84
5/1/84	5/3/84	5/4/84
5/11/84	6/20/84	6/26/84, 7/5/84
5/24/84	6/22/84	6/26/84
9/17/84-10/14/84	10/16/84	12/20/84, 12/21/84

Florence S. Gilson
Florence S. Gilson
Assistant Supervisor of
Quality Assurance

12-21-84
Date

92 JUN 13 AM 9:50

CERTIFICATE OF AUTHENTICITY

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